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Conjunctival Squamous Cell Carcinoma Due to Ocular Prostheses: A Case Report and Review of Literature

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Abstract Conjunctival squamous cell carcinoma (SCC) is a rare finding in everyday clinical practice, but is the most common malignancy of the ocular surface. The incidence of this malignancy in the United States is 0.03 per 100,000 persons. It is one extreme of a spectrum of lesions encompassed in ocular surface squamous neoplasia which range from dysplasia to carcinoma in situ to invasive SCC. Exposure to ultraviolet radiation B (UVB), human papilloma virus (HPV), and human immunodeficiency virus (HIV) infection of eroded ocular surface are important risk factors predisposing to the development of this malignancy. Herein we report a case of SCC arising in chronic conjunctival irritation due to prolonged prosthetic use following enucleation for traumatic eye injury.

Keywords Conjunctiva · Squamous cell carcinoma · Prostheses

Introduction

Conjunctival SCC is the most common form of conjunctival malignancy though such lesions are rarely seen in everyday practice. The incidence of SCC of the conjunctiva worldwide is 0.02 to 3.5 per 100,000 [1]; while in United States it is 0.03 per 100,000 persons [2]. It is one extreme of a spectrum of lesions encompassed in ocular surface squamous neoplasia, which range from dysplasia to carcinoma in situ to invasive SCC [3]. This disease has characteristic predominance in Caucasian elderly men and originates the majority of the times at the limbus in the interpalpebral zone [4, 5]. Clinically, it is difficult to differentiate SCC from conjunctival intraepithelial neoplasia; this distinction is based on invasion of the epithelial basement membrane and underlying stroma [4]. SCC typically presents as a slow growing mass macroscopically described as gelatinous, velvety or papilliform, leukoplakic, nodular, and diffuse at the limbus with a chief complaint of irritation or redness of the eye [1].

The risk factors for conjunctival SCC tumor include actinic damage due to excessive exposure to the ultraviolet radiation, chronic irritation and infectious agents like trachoma, HPV 16, 18, and HIV. While a majority of these tumors are seen in the elderly, the presentation of SCC of the conjunctiva in immunocompromised individuals is mostly in young individuals. It is also associated with chronic inflammatory diseases like chronic blepharoconjunctivits and atopic eczema. Systemic diseases causing immune suppression like hematologic malignancies and organ transplantation have also been shown to increase the incidence. Surface microtrauma causes surface ulcerations and increases the chances of infections in conjunctiva [2, 6]. It is hypothesized that the T-cell dysfunction in these associated conditions mediates the malignant transformation of the conjunctival epithelium [4]. It is considered as a low grade malignancy with good prognosis. It may be locally invasive but only 5% show local recurrence and less than 2% have regional metastases [4].

Conjunctival SCC arising of chronic irritation to the conjunctiva due to ocular prostheses has been reported in only six cases in world literature in the English language. We herein report a case of invasive SCC of the conjunctiva, which developed after many years of ocular prosthesis use and without any other known risk

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factors. We also review the existing literature on the topic.

Clinical History

A 60-year-old man presented with a significant past medical history of loss of right eye post injury 53 years back. He was hit in the eye with a slingshot after which a right eye enucleation was performed. Since then, he has used multiple prostheses for this eye. Apart from mild irritation and ulceration in that orbital area, the patient did not complain of any major symptoms until one month before his presentation to the clinic. He presented with progressive and worsening swelling and edema of right upper and lower eyelids with pain in the right orbit, which had progressed to the stage where he was unable to keep the prosthesis in his right eye. Before seeking attention at our medical center, he treated with a round of oral antibiotics without significant improvement. Ophthalmologic examination at his first visit here revealed periorbital cellulites and erythematous orbit with no evidence of any discharge and lymphadenopathy. An excisional biopsy of the right eye demonstrated moderately differentiated conjunctival keratinizing SCC with no evidence of perineural or vascular invasion. Following the pathology report, magnetic resonance imaging (MRI) of the brain was performed to rule out intracranial extension. The report showed enhancing, necrotic appearing right orbital mass with evidence of inflammation. The MRI of right orbit showed noticeable enhancement of the soft tissue surrounding the anterior orbit, orbital septum, insertion of extraocular muscles, superior and inferior eyelid, and medial and lateral canthus with subtle enhancement extending along the proximal optic and oculomotor nerve. Other systemic evaluation for metastasis was negative. The patient had positive history for chronic conditions like Type 2 diabetes mellitus, hypertension, and hypothyroidism. The patient was a smoker but has quit smoking for 33 years now. He consumes alcohol occasionally. He is currently unemployed and pursuing further education.

Material and Methods

The patient underwent a major right eye exenteration with medial and lateral orbital wall biopsies. Pathology specimen received consisted of a mass measuring 7.4×4.3×4.2 cm. The facial skin including eyebrows and eyelids were grossly free of disease. Sectioning of specimen in the sagittal plane revealed a 3.5×3×2.2 cm tan-white, firm, somewhat well circumscribed mass that grossly appeared to abut the overlying skin of the upper eyelid. The tumor predominantly involved the "bulbar" conjunctiva with secondary involvement of the palpebral conjunctiva as shown in Fig. 1. Grossly, the tumor was thought to be 0.5 cm from the superior soft tissue margin, 0.8 cm from the inferior soft tissue margin, and at least 1 cm from the remaining soft tissue margin.

Results

Histological sections show a moderately differentiated keratinizing SCC arising from the conjunctiva (Fig. 2). The orbital bone specimen showed reactive changes but no evidence of malignancy. There was no evidence of intracranial invasion. Postoperatively, he was recommended a course of radiation therapy to decrease the risk of local recurrence.

Discussion

Individuals with loss of an eye or disfigurement use ocular prostheses. These prostheses help them in getting professional and social acceptance. However, there are problems associated with the use of these ocular prostheses. Patients who have used ocular prostheses for a long period of time complain of ptosis, ectropion/lid laxity and socket contraction [7]. Apart from these benign changes, few individuals experience dysplastic changes of the conjunctiva with chronic use of ocular prostheses, which can further progress to invasive SCC. Kim et al. observed the occurrence of squamous metaplasia in anopthalmic conjunctival sockets with reduction in goblet cell density and increase in nucleus to cytoplasm ratio [8]. Thus,

Fig. 1 Gross appearance of the conjunctival tumor postexenteration. Note the white-tan tumor in the superior region of the specimen abutting the upper eyelid

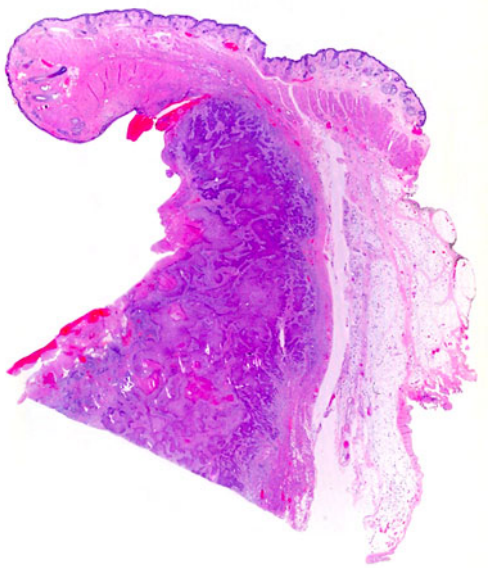

Fig. 2 Low power microscopic appearance at 1X magnification of the whole section showing the tumor area and the surrounding normal tissue

it could be hypothesized that in an anophthalmic eye, history of prolonged usage of ocular prostheses gives rise to dysplastic changes due to chronic conjunctival irritation ultimately leading to invasive SCC of the conjunctiva. These well differentiated tumors are histologically characterized by eosinophilic cytoplasm, keratin pearls, intercellular bridges, and mild pleomorphism [9]. SCCs should be distinguished from giant papillary conjunctivitis, which is also associated with chronic use of ocular prostheses [10]. This lesion is a resultant of combined inflammatory and allergic response to deposits on ocular prosthesis in upper tarsal conjunctiva. Impression Cytological examination reveals the presence conjunctival infection, mucosal strands and honeycombed appearance of the epithelial clusters consistent with giant papillae. While most of these lesions remain asymptomatic, cases have been observed presenting with irregular thickening, proliferation or atrophy of the conjunctival epithelium [10]. Thus, while lesions of the conjunctiva associated with chronic prosthetic use may be limited, conditions like Bowen disease, basal cell carcinoma, squamous papilloma, sebaceous cell carcinoma, inverted follicular keratosis, and seborrheic keratosis could arise due to other causes in the conjunctiva [9]. These conditions should be appropriately ruled out before making a diagnosis of SCC.

While the SCC in this case arose from chronic prosthetic use, the most common risk factor of this lesion is exposure to UVB. Fair skinned people exposed to UVB are particularly at risk for this type of malignancy [11]. It is more common in the tropical regions. Newton et al. have demonstrated that the risk of this lesion reduces by 49% for every 10° increase in latitude [3]. Premalignant lesions such as actinic keratosis, SCC in situ and genetic disorders like xeroderma pigmentosum and albinism also predispose for invasive SCC [9]. Our patient does not have occupation or nonoccupational exposure to excessive ultraviolet radiation. Similarly, he did not have any signs or symptoms to suggest conditions like xeroderma pigmentosa. The patient lives 30° in latitude away from the equator and currently unemployed.

HPV types 16 and 18, and HIV have also been found to be associated with conjunctival neoplasms [12]. HPV can also be detected in conjunctiva of noncancerous and normal patients with polymerase chain reaction. Due to this observation, it is suggested that HPV could be a secondary invader and not the primary cause of conjunctival neoplasms and attempts to isolate the HPV DNA in malignancy have been unsuccessful [6, 13]. The HPV assay was not conducted on our patient since its importance in conjunctival neoplasms due to ocular prostheses use has not been adequately demonstrated. There were no risk factors for HIV infection in our patient. Other risk factors for SCC of the conjunctiva include arsenic and polyhydrocarbons exposure, smoking, and immunosuppresstion after renal transplantation [9]. All these risk factors have been successfully ruled out in our patient.

Table 1 Summary of published literature on 'conjunctival SCC arising of chronic prosthetic use'

Study	Year	No. of cases	No. of yrs of prosthetic use	Findings
Hsu et al. [14]	2009	1	63 yrs	SCC of conjunctiva involving left socket; locally invading into superior and lateral rectus muscle, preseptal soft tissues, and lacrimal fossa
Nguyen et al. [2]	2008	2	>40 yrs	SCC of posterior cul-de-sac conjunctiva and extension in deep orbital tissues; eyelid skin and palpebral conjunctival sparing
Chaudhry et al. [15]	2006	1	>50 yrs	SCC of the conjunctiva involving the left orbital socket; several bleeding points noted
Endo et al. [16]	2006	1	40 yrs	SCC of the lower eyelid with metastases to submandibular lymph nodes
Whittaker et al. [5]	2002	1	49 yrs	SCC of lower palpebral conjunctiva
Campanella et al. [17]	1998	2	>40 yrs	SCC of upper palpebral conjunctiva; parotid gland metastases in one case

We have described a patient suffering from invasive conjunctival neoplasm due to chronic irritation after wearing the ocular prostheses for 53 years. Apart from this current case, there have been eight reported cases of SCC involving an anophthalmic orbit in world literature in the English language; these have been briefly summarized in Table 1. All cases described have been associated with chronic irritation of the conjunctiva due to ill fitting ocular prostheses and is suggested as an etiological agent in the development of conjunctival SCC.

In conclusion, our report, as well as previous reports, adds to the evidence that there could be an association between chronic irritation due to prolonged use of ocular prostheses and the development of conjunctival SCC. Regular checkup of the prostheses as well as the education to the patients is prudent to avoid this condition.

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