Squamous Cell Carcinoma of the Cornea and Conjunctiva Treated by Surgical Excision and a Combination of MMC and 5-FU Eye Drops: Case Report

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Abstract

Squamous cell carcinoma of the conjunctiva (SCC) is considered as one of the ocular surface squamous neoplasia (OSSN). It is the most common conjunctival malignancy. In this report, we describe the short term success of surgical excision, followed by topical chemotherapy, with 5-fluorouracil (5-FU) and mitomycin C (MMC) eye drops, in a 43-year old Egyptian woman.

Keywords: Ocular Surface Squamous Neoplasia; Surgical Excision; Topical Chemotherapy

Abbreviations

5-FU: 5-Fluorouracil; BSS: Balanced Salt Solution; CIN: Conjunctival/Corneal Intraepithelial Neoplasia; H&E: Hematoxylin and Eosin; HIV: Human Immunodeficiency Virus; HPV: Human Papilloma Virus; MMC: Mitomycin C; OSSN: Ocular Surface Squamous Neoplasia; SCC: Squamous Cell Carcinoma

Introduction

Ocular surface squamous neoplasia (OSSN) encompasses a wide and varied spectrum of disease involving abnormal growth of dysplastic squamous epithelial cells on the surface of the eye, ranging from epithelial dysplasia, conjunctival/corneal intraepithelial neoplasia (CIN) to invasive squamous cell carcinoma (SCC) [1,2]. CIN is a slow-growing tumour that has not invaded the basement membrane of the conjunctival or the corneal epithelium. Once the dysplastic epithelial cells penetrate the basement membrane it is called invasive SCC, and will have a metastatic potential [3,4].

OSSN is usually unilateral and occurs in middle aged to elderly patients. Bilateral OSSN is rare, but has been reported in immunocompromised patients [5]. The prevalence of OSSN varies widely according to race and geographic area. It ranges from 0.3 to 8.4 per million per year in United States [6,7] and is much higher in Africa, 35 cases/million/year (Uganda, 1992) [8,9]. CIN has been reported to be the most common conjunctival neoplasy and SCC has been found to be the most common conjunctival malignancy [10]. The aetiology of OSSN appears to be a multifactorial and related to sun exposure, male gender, age and viral infection such as human papilloma virus (HPV) and human immunodeficiency virus (HIV) [11-14]. Although conservative medical approaches has been progressively increasing in recent years, surgical excision is still the gold standard method for treatment [3,15].

Purpose of the Study

The purpose of this report was to describe a short term success of surgical excision of a squamous cell carcinoma of the conjunctiva and the cornea after receiving a combination of 5-fluorouracil (5-FU) and mitomycin C (MMC) eye drops.

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Materials and Methods
A 43-year-old Egyptian woman presented with squamous cell carcinoma of the conjunctiva and the cornea of the right eye. She gave a history of surgical excision of a pterygium few years before. Complete clinical examination and slit lamp photography were performed pre- and postoperatively. Surgical excision of the tumor under general anesthesia was done followed by chemotherapy with topical 5-FU and MMC eye drops. Histopathology of the excised lesion was performed before treatment with chemotherapy.

Case Report and Discussion
A 43-year-old lady presented with a roughly oval 7 X 5 X 3 cm mass on the nasal palpebral conjunctiva of her right eye. The mass had roughened lobulated surface and was surrounded by heavy vascularization and was firmly attached to the underlying tissues (Figure 1). Surgical excision of the mass was done under general anesthesia after complete clinical examination and color photography on slit lamp biomicroscopy. The surgical steps are illustrated in Figure 2. The first step was cautery demarcation of the area which needs excision (Figure 2A), followed by separation of this area from the conjunctiva by scissors (Figure 2B). Lamellar dissection with a crescent knife to separate the lesion from the underlying tissue was done (Figure 2C). Further cautery was performed as needed (Figure 2D) then final excision of the mass was done (Figure 2E). A bare sclera was left. Bandage contact lens was used at the end of surgery to help epithelialization of the cornea and to decrease the postoperative discomfort (Figure 2F).

Figure 1: Representative colour slit-lamp photographs of a conjunctival lesion invading 2 mm of the cornea at the 4 O’clock with vascularization at nasal and inferior boundaries.

Figure 2: Steps of surgical excision. (A) Cautery demarcation. (B) Scissors Separation. (C) Knife lamellar dissection. (D) Further cautery. (E) Final excision. (F) Bandage contact lens.

Postoperative treatment included topical Moxifloxacin hydrochloride 0.5% (Vigamox; Alcon Laboratories Inc., Fort Worth, Texas, USA) eye drops 5 times a day for 5 days and preservative free artificial tears every hour during the waking hours for 2 months. A topical combination of Tobramycin and Dexamethasone eye drops (Tobradex; Alcon Laboratories Inc., Fort Worth, Texas, USA) was started after 5 days and bandage contact lens removed after complete epithelial healing of the cornea. The excised mass was sent for histopathological evaluation and revealed invasive squamous cell carcinoma on top of CIN showing pleomorphism, squamous pearls, multiple mitosis, dyskeratosis and multinucleated cells (Figure 3-5). Topical chemotherapy was started after confirmation of diagnosis with histopathology examination. It included MMC 0.02% four times per day for 14 days in 2 cycles 1 week apart, 5-FU 1% four times per day for 4 weeks, and topical combination of Tobramycin and Dexamethasone eye drops (Tobradex; Alcon Laboratories Inc., Fort Worth, Texas, USA) three time per day for 2 months. Preparation of topical chemotherapeutic eye drops was carried out by a local senior pharmacist (RFM), under sterile conditions. He used Balanced Salt Solution (BSS) to dilute MMC (Zydus Oncosciences; IndiaMART, InterMESH Ltd., India) 2 mg vial to reach 0.04% concentration in a dropper bottle of 15 ml. For 5-FU (Sandoz; International GmbH, Germany), he diluted a 50 mg ampule using BSS to reach 1% concentration in a dropper bottle of 15 ml. The conjunctiva and cornea healed completely within 2 months (Figure 6b). No evidence of recurrence during period of follow up (5 months). Figure 6 shows the postoperative photographs of the case at the first day (Figure 6A) and after one month of chemotherapy and steroid therapy (Figure 6B).
Histopathological evaluation of OSSN remains the gold standard for the diagnosis following an incisional or excisional biopsy [16]. Depending on the histopathological findings, when neoplastic cells invade through basement membrane, the conjunctival squamous neoplasia is considered as invasive SCC [17]. Modalities of treatment of OSSN includes surgical excision [18], topical chemotherapy (MMC, 5-FU), topical/local immunomodulation with interferon alpha-2b, topical antiviral medications (cidofovir) [19] and photodynamic therapy [20]. Treatment with anti-vascular endothelial growth factor has also been tried, with inconsistent results [21].

Surgical excision is still the gold standard method for treatment. A no touch technique is used during excision of OSSN lesions. A large conjunctival margin is important because it may still contain dysplastic cells. Absolute alcohol can be used to loosen corneal epithelium from the basement membrane, and then rinsed off with copious irrigation. Cryotherapy is important as it effectively extends the surgical margins. Topical chemotherapy may be used after excision, if the margins return positive or there are any concerns for residual disease. A thin lamellar scleral flap after the removal of the conjunctival lesion is advised in cases of SCC [3,15].

The prognosis of OSSN ranges from good to fair, with a low mortality rate and low tendency to metastasize [22]. However, the risk of recurrence after treatment has been reported in the literature to be up to 39% [23,24] and this rises to 43% when treated exclusively.

with surgery or solely with topical agents [25,26]. Many factors affect the recurrence rate such as the involvement of surgical margins, the presence of feeder vessels, histopathologic grade, HIV infection, and the adjunctive cryotherapy, immunotherapy or chemotherapy [3,23,27-30].

Conclusions
A combination of surgical excision, and topical MMC and 5-FU were successful in the eradication of a highly aggressive squamous cell carcinoma of the cornea and conjunctiva for 6 months. However long term follow up is necessary to judge the ultimate outcome.

Conflict of Interest
There is no financial interest or any conflict of interest.

Acknowledgement
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Bibliography

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