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#### MANAGEMENT OUTCOME OF OCULAR SURFACE CONJUNCTIVAL NEOPLASIA

E. Ackuaku-Dogbe, DO, FWACS, FGCPs, Senior Lecturer, University of Ghana, School of Medicine and Dentistry, Department of Surgery, Eye Unit, Consultant Ophthalmologist and B. Quaye, MGCPs, Specialist Ophthalmologist, Eye Unit, Korle-bu Teaching Hospital, P.O. Box 4236, Accra

Request for reprints to: Dr. E. Dogbe, University of Ghana School of Medicine and Dentistry, Eye unit, Department of Surgery, P. O. Box 4236, Accra, Ghana, E-mail: edithdogbe@gmail.com

## MANAGEMENT OUTCOME OF OCULAR SURFACE CONJUNCTIVAL NEOPLASIA

E. ACKUAKU-DOGBE and B. QUAYE

### ABSTRACT

**Background:** Ocular surface squamous neoplasia (OSSN) are a spectrum of lesions that arise from the squamous epithelium of the conjunctiva and cornea. They form the most frequent indication for orbital exenteration in Korle-bu Teaching Hospital, Accra. Poor management of early lesions leads to high rates of tumour recurrence and extension to adjacent structures.

**Objective:** To determine the management outcome of combined surgical excision followed by topical 1% 5-fluorouracil (5-FU) in patients presenting with early OSSN limited to the ocular surface.

**Design:** retrospective clinical study

**Setting:** Korle bu Teaching Hospital, Accra, Ghana

**Subjects:** The records of all patients who presented with OSSN at the eye clinic of Korle-bu Teaching Hospital, Accra between May 2013 and June 2014 were reviewed retrospectively. Data on age, sex, HIV status, histology results and treatment outcome were recorded and analysed.

**Results:** The mean age of patients was 43.2 ±12.17 years (range-18 to 59 years). At 6 weeks of follow up, all 18 patients seen were clinically free of tumour. At six months of follow up seven (33.9%) patients had defaulted and there was one (5.6%) recurrence. The main complication was corneal epithelial keratitis which resolved following cessation of topical 5-FU

**Conclusion:** Ocular surface squamous neoplasia is effectively treated with excision and application of 1% 5 Fluorouracil with minimal side effects. The drug is readily available and affordable. However, a longer duration of follow up is required to adequately evaluate long term recurrence rates.

### INTRODUCTION

Ocular surface squamous cell carcinoma (OSSC) is the most common malignancy of the ocular surface. In developing countries, the tumour behaves in an aggressive manner. Delays in management and lack of expertise in management of early disease can lead to extension of the tumour into the adjacent structures requiring disfiguring surgery or even resulting in death from metastatic disease or invasion of adjacent structures. In a review of exenterations performed in Korle-bu teaching hospital, out of 25 patients who underwent orbital exenteration, 19 (76%) were for invasive orbital squamous cell carcinomas from the

ocular surface. A good proportion of these patients (6%) had had previous surgeries for earlier stages of conjunctival lesions ranging from single or multiple excisions to evisceration and enucleations. This highlights some of the problems faced in managing early cases of OSSC in peripheral hospitals in Ghana. Various methods of managing the localised disease have been described. These include surgical, medical and a combination of both. Some of the drugs for medical treatment are not available or are unaffordable for the average patient in developing countries. Our aim was to determine the outcome of use of topical 1% 5 Fluorouracil (5-FU) as an adjunct to surgical excision in patients attending the eye

clinic of the Korle-bu teaching hospital, a tertiary referral hospital.

### MATERIALS AND METHODS

This was a retrospective study of patients with ocular surface squamous neoplasia (OSSN) treated at the eye clinic of the Korle-bu Teaching Hospital, Accra between May 2013 and June 2014. Patients with tumours extending beyond the ocular surface were excluded. The standard treatment of these patients was excision of tumour with or without conjunctival cover over bare sclera. Topical 5-FU 1% reconstituted in tear substitutes (normo-tears), was started two weeks post operation in all but one patient. In one patient topical 5FU was started on the day of surgery. Adjuvant treatment with topical antibiotic-steroid combination (maxitrol) was given to control inflammation. Treatment was continued for four weeks in 16 (88.9%) patients. In one patient treatment was suspended at two weeks on account of worsening of epithelial disease until the epithelial defect resolved

and then continued for two more weeks. In another patient the treatment was discontinued completely as the patient developed suppurative keratitis. The case notes of these patients were retrieved and data on age, sex, HIV status, histology of tumour, and treatment outcome were recorded and analysed. Outcome was presented as counts and percentages.

### RESULTS

Patients' demographic data and tumour characteristics are shown in Table 1. The total number of patients included in the study was 18. The age range was 18 to 59 years ( $\pm 12.17$ ) with a mean of 43.2 years. The M:F ratio was 1:2. Histology records of 14 (77.8%) were retrieved and confirmed tumours as OSSN. Histology records for four patients could not be retrieved. Tumour size ranged from 1 clock hour to about 10 clock hours with majority (66.7%) between 1-3 clock hours. Sixteen (88.8%) out of the 18 patients had corneal involvement of the tumour.

**Table 1**  
*Patient and tumour characteristics*

| Patient Characteristic | Number | Percentage |
|------------------------|--------|------------|
| SEX                    |        |            |
| Male                   | 6      | 33.3       |
| Female                 | 12     | 66.7       |
| HIV STATUS             |        |            |
| Negative               | 7      | 33.9       |
| Positive               | 7      | 33.9       |
| Not known              | 4      | 22.2       |
| TUMOUR SIZE            |        |            |
| 1 to 3 clock hours     | 12     | 66.7       |
| 4 to 6 clock hours     | 5      | 27.8       |
| >6 clock hours         | 1      | 5.6        |

All patients except one had complete excision of the tumour prior to topical 5-FU. Only one patient commenced topical 5-FU on day of surgery. The rest started two weeks after surgery.

The most common complication was corneal epithelial defects which occurred in five (27.8%) patients at two weeks. One patient developed suppurative keratitis. This was the patient who commenced topical 5-FU on day of surgery. All epithelial defects and suppurative keratitis were successfully managed.

Follow up period was between six weeks and ten months. At six weeks after excision and topical chemotherapy, all patients were found to be free of

local tumour. At ten months only 11 (61.1%) of the 18 patients were seen at follow up. Of these ten (90.1%) were tumour free; only one patient had tumour re-growth. This patient had bilateral disease and had limited exenteration in the right eye. The left eye had excision with topical 5-FU but had re-growth of tumour at a different site from the site of initial treatment in the left eye. He was HIV sero-negative.

### DISCUSSION

In the past, treatment for OSSN has been surgical, and later surgery combined with cryotherapy to the conjunctival wound edges. However non-surgical

interventions have been increasingly adopted as it was soon realised that microscopic disease may extend beyond the edge of the clinically identified disease (5). Recurrence rates with surgical excision with or without cryotherapy have been high, about 33% even in cases with clear margins on pathology specimens (5). For this reason, excision is currently combined with topical chemotherapy or cryotherapy (6).

5-FU is a pyrimidine analogue that is structurally similar to thymidine and uracil. The drug acts by blocking DNA synthesis, therefore inhibiting cells in the S-phase of the cell cycle, as well as by being incorporated into RNA and interfering with its synthesis. The drug is synthesised and has been used to treat many epithelial cancers because of its actions on rapidly proliferating cells. 5FU is stable in aqueous solution even without refrigeration.

In this study, the patients were treated with surgical excision followed by topical chemotherapy with 1% 5FU. The two week period post operation before commencing topical chemotherapy was to allow the ocular surface to heal. Success rate of tumour clearance at the primary site was over 90% for the 60% of patients who were seen at follow up at ten months. In a study by Edoardo and others, eight patients with conjunctival squamous cell carcinoma (three recurrent cases, three incompletely excised, and two untreated cases) were treated with 1% 5-FU eye drops four times daily for four weeks. After a mean follow up of 27 months all patients showed clinical regression with normal conjunctival epithelium within three months. In a study by Raffaele, Parrozzani and others (9), topical 5-FU was used in the treatment of 22 patients as a sole treatment, and in another 19 patients as adjuvant to excision or debulking therapy. Three tumours (7.3%) treated with 5-FU alone recurred during mean follow-up period  $89.7 \pm 14.4$  months. This study suggests that results for treatment with topical 1% 5FU are better when combined with excision or debulking than with chemotherapy alone.

Several treatment modalities have been defined for the management of OSSN but not all are convenient or affordable in the developing world. These include surgery alone or in combination with topical or subconjunctival injections of anti-cancer agents. Apart from 5FU, mitomycin C (MMC) and interferon  $\alpha 2b$  (IFN- $\alpha 2b$ ) have been successfully used. However MMC and IFN- $\alpha 2b$  are expensive and complication rates with MMC are much higher and more severe than with 5FU. MMC (0.04%) has been shown to cause disruption of the limbal stem cells that may result in chronic ocular surface disorders with corneal haze in some patients (9). In this study about 27% of patients had epithelial defects. These were treated with discontinuation of chemotherapy and use of tear substitutes and topical steroids. In a study involving 55 patients treated with topical

5FU, 57% of patients had short-term complications. The main complications recorded were eye lid toxicity, superficial keratitis, epiphora and corneal epithelial defects; four patients were unable to complete the course of 5-FU 1% because of local toxicity. This study confirms the effectiveness and low toxicity of 1% 5FU used in the treatment of localised OSSC.

There does not seem to be a good knowledge of management of the early disease by general ophthalmologists in the peripheral hospitals in developing countries. In a previous study (4) we reported that of 25 patients who underwent orbital exenteration in Korlebu teaching hospital, 19 (76%) were for invasive orbital squamous cell carcinomas from the ocular surface. Six percent of these patients had had previous surgeries for earlier stages of conjunctival lesions ranging from single or multiple excisions to evisceration and enucleations.

In conclusion, this study confirms that local excision of OSSC with adjuvant 5FU is effective and can be successfully employed in developing countries. It is our hope that further prospective studies with a larger sample size and longer follow up period would prove the use of topical 5FU an effective and affordable adjuvant treatment to local excision in the developing world. Dissemination of this information should prevent morbidity and mortality from this condition.

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