

A Report of Three Cases of Ocular Surface Squamous Neoplasia Treated with 5-Fluorouracil Drops

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Abstract

Objective: To raise the awareness of the use of topical 5-fluorouracil in management of recurrent ocular surface squamous neoplasia.

Methods: A case series study carried out at an Ophthalmic clinic, in Western Nigeria. The subjects were managed for ocular surface squamous neoplasm. **Results:** Three patients aged 31–52 years were seen in the period of study. They were operated upon and early recurrence was noted in them. 5-Fluorouracil eye drop was used in the management of recurrent tumor with good results. **Conclusion:** There was good response with the use of topical 5-fluorouracil for the management of recurrent ocular surface squamous neoplasia.

Keywords: 5-Fluorouracil, recurrence, ocular surface squamous neoplasia

INTRODUCTION

Ocular surface squamous neoplasia (OSSN) encompasses a group of disorders from mild dysplasias to intra epithelial neoplasia and invasive squamous cell carcinoma of the conjunctiva and cornea. They are usually difficult to distinguish from one another. In the non-neoplastic diseases, the basement membrane is intact but it is breached in neoplastic lesions. It is less common when compared to oculo-orbital tumors.^[1] Incidence is high among Africans^[2,3] with no sex predilection.^[2] Most of the lesions arise from the limbal stem cells in the nasal quadrant^[4] and are often unilateral.

Systemic review and meta-analysis have shown strong association of OSSN with ultra violet irradiation, Human Papilloma Virus, and human immune deficiency virus infections.^[5] They typically appear as gelatinous, papilliform, leukoplakic, localized, or diffused lesions at the limbus. They may be raised or flat and in most cases, well demarcated from the surrounding tissues. Feeder vessels may also be seen.^[1] They tend to be located in the interpalpebral fissure and straddle the adjacent limbus.^[1] Diagnosis can be made clinically but definitive diagnosis is made histopathologically through impression cytology and biopsy. Management is surgical, conservative, or a

combination of both. Conservative management with Interferon alfa-2b (IFN- α_{2b}), Mytomycin C (MMC), 5-fluorouracil (5-FU) has gained popularity.^[4]

It has high recurrence rate^[6] ranging from 15% to 52%.^[1] In their review of OSSN, recurrences were higher in severe grades and did not depend much on the status of the surgical margins.^[6] In another article however, greater recurrence was related to the surgical margin.^[3] Most lesions were found to reoccur within 2 years of excision.^[7] The recurrence tends to follow perforating vessels on the surface of the eye, causing iritis, inflammation, glaucoma, retinal detachment, and scleral thinning. Metastasis could be to the regional nodes (submandibular, preauricular, and cervical lymph nodes), lungs, and bones.^[7] Both intraoperative and postoperative adjuvant therapies have been used to prevent recurrence.

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Prevention of recurrence has been tried with varying modalities of treatment such as chemotherapy with agents like 5-fluorouracil, mytomyacin C (MMC), interferon alfa-2b (IFN α_{2b}), radiotherapy, cryotherapy, immunotherapy with dinitrochlorobenzene and, excisional biopsy.^[1,4]

This study aims to enhance the knowledge of management of ocular surface squamous neoplasia with 5-fluorouracil drops. There is also, dearth of data on this subject matter in our locality.

MATERIALS AND METHODS

The study was conducted in an ophthalmic facility located in Western Nigeria.

This was a retrospective, descriptive study of three cases of ocular surface squamous neoplasia seen between 2017 and May 2018. The case files of the patients were retrieved and information such as the biodata, clinical presentation, eye examination findings, histology reports, and management of these cases were extracted. In each case, clinical examination was carried out after obtaining a detailed history. Ophthalmological assessment included routine ocular examination with special reference to the ocular surface lesions.

The same surgical procedure was performed in the three patients. The tumors were excised along with 2 to 4 mm macroscopically tumor free conjunctiva margin. The tumors were not attached to the sclera bed or the cornea.

Immediate postoperative treatment consisted of chloramphenicol eye drop, one drop three times daily for 3 weeks, dexamethasone eye drop, one drop three times daily, tailed off within 5 to 6 weeks, and meloxicam tablets, 7.5 mg daily for 3 days.

The 1% 5-FU was constituted by diluting 1 ml of 50 mg/ml solution with 4 ml of water for injection.

Case Reports

Case 1

A 52-year-old female trader presented with one and half-year history of slowly growing mass in the inner aspect of the left

eye. The growth was accidentally discovered in a general hospital. There was no previous ocular surgery or trauma, no associated redness, discharge, or decrease in vision. She was not a known HIV positive or diabetic patient. Ocular examination revealed an essentially normal right eye. The left showed a gelatinous, papilliform, leucoplakic conjunctival mass, astride the cornea, with feeder vessels [Figure 1]. There was no regional lymphadenopathy. Histological diagnosis of conjunctival intraepithelial neoplasia was made following the excisional biopsy. Two weeks following excision, recurrence was observed. A gelatinous mass was seen growing on the bare sclera. This necessitated topical application of 1% 5-fluorouracil, one drop, three times daily for 4 weeks.

There were no adverse effects. Patient was followed up for at least 4 years, without recurrence.

Case 2

A 45-year-old female civil servant who presented with 3-month history of a growth in the inner aspect of the left eye. It was painless and not associated with itching or bleeding and, was slowly growing. She was a known HIV positive patient on highly active antiretroviral therapy (HAART) but not diabetic. On examination, the general condition was satisfactory and no regional lymphadenopathy. The right eye was essentially normal. Visual acuity in both eyes were 6/9. The left showed a nasally located interpalpebral conjunctival mass which was gelatinous, leucoplakic, papilliform, with prominent feeder vessels. The mass was overriding the nasal aspect of the cornea. Histological diagnosis of basaloid squamous cell carcinoma following an excisional biopsy was made.

Fourth day after excision, a gelatinous mass was seen growing on the scleral bed. She was commenced on 1% topical 5-fluorouracil, one drop three times daily, after which the growth started regressing. By the 27th day of the topical application, punctate keratitis was observed necessitating withdrawal of the drop application. By 2 years post treatment when the patient was last seen, the tumor had not reoccurred.

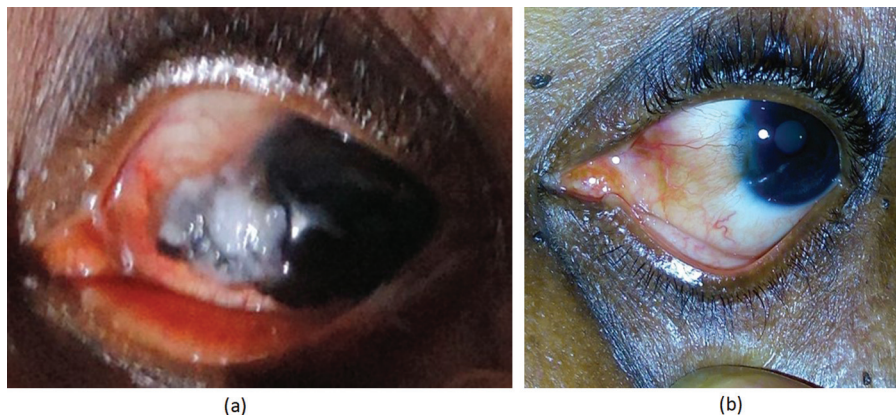


Figure 1: A 52-year-old woman with nasal conjunctival mass astride the cornea before treatment (a). Four years post treatment, no recurrence (b).

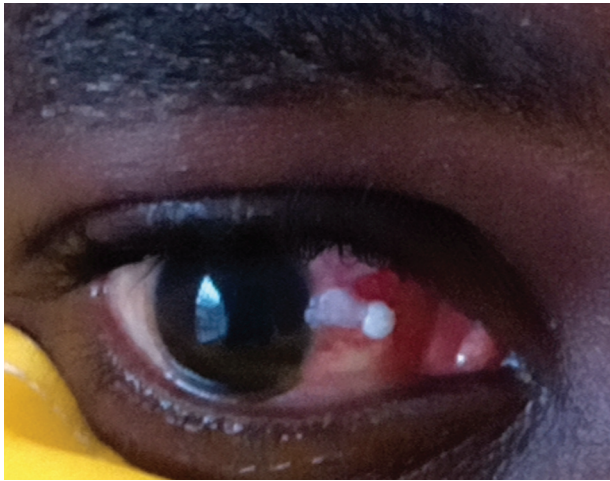


Figure 2: A 31-year-old man with right nasal conjunctival mass.

Case 3

A 31-year-old male trader who presented with a 2-day history of growth in the inner aspect of the right eye. The growth was not itchy and there was no discharge. He did not observe swelling in any other part of the body and not a known HIV or diabetic patient. On examination, the patient's general condition was satisfactory with no regional lymphadenopathy.

Abnormal finding was in the right eye which showed a deeply vascularized, raised, leucoplakic, gelatinous, papilliform mass arising from the nasal conjunctiva and extending to the limbus [Figure 2].

Excisional biopsy was carried out, with application of 50 mg/ml 5-fluorouracil to the tumor bed intraoperatively. By the 5th day postoperatively, increased vascularization of the surgery bed was observed. He was commenced on topical 1% 5-FU, one drop three times daily for a period of 4 weeks. No complications were observed. Histological diagnosis of conjunctival intraepithelial neoplasia with atypia was made. By 10 months postoperatively when he was last seen, there was no recurrence.

DISCUSSION

Three cases of ocular surface squamous neoplasia at different stages were presented. The duration of the presentation ranged from 2 days to one and half years. Delay in presentation in two of the patients could have been due to: waiting time in the hospital, cost, distance and non-availability of health care facilities^[8] and, perceived non-seriousness of the health condition.^[9] Slow growth of the tumors and ignorance could also be responsible as observed in one of the patients who was not even aware of the problem till she visited a health institution. There was no physically detectable regional lymphadenopathy which could imply spread. The age ranged from 31 to 52 years. In a major review of ocular surface squamous neoplasia, the average age reported was 41 years,^[6] but in Eastern and Southern parts of

Africa it was found commonest in young persons in their 30s.^[2] The physical appearance of all the tumors were typical of ocular surface squamous neoplasia. The recurrences in the study in the first two cases were clinically diagnosed, and appeared as raised, pale lesions with gelatinous appearance noted on the surgery beds.

Patients were followed up for a period of 10 months to 4 years without physically observable recurrence. For one of the patients, intraoperative 5-FU was given, but for all three, 1% of the solution was given three times daily for 4 weeks in two of the patients and 27 days in one. The increased hyperemia observed in one patient necessitated the commencement of the drops postoperatively. The primary treatment of OSSN by surgical excision including tumor free margins tends to have high rate of recurrence. Different modalities of treatment have been applied in the management of OSSN but the most popular were 5-fluorouracil, mitomycin C, and interferon- α 2b (IFN- α 2b).^[4] 5-FU has been recommended for effective treatment of the primary lesions^[10] as well as recurrences.^[6] In the current presentation, three categories of the tumor were seen in the three patients. They all showed signs of recurrence and were treated with the 1% 5-FU drops. Several studies have also shown reduced recurrence of the tumor with the drop.^[4,6,11] Different regimen were applied. Only one person showed complication requiring discontinuation of the drop after 27 days. The complications reported by Joag *et al.*^[11] included redness, irritation, limbal stem cell deficiency, diplopia, symblepharon, etc. In this study, the shortest follow up duration was 10 months. It was assumed that the patient did not see the need for checkup because he judged the problem resolved.

All patients had histological diagnosis of OSSN and showed recurrence shortly after excision. They all responded well to topical treatment with 1% 5-fluorouracil without tumor recurrence for the period of follow up. It is recommended that a greater number of patients be managed with this approach and followed up for at least 2 years.

Limitations of the Study

Diagnosis of recurrence and non-recurrence were made by clinical observation only, there was no repeat of histological examination because of financial constraint. One of the patients was followed up for only a short period of 10 months and the number of patients was small.

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Conflicts of interest

There are no conflicts of interest.

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