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Case Report

Treatment of ocular surface squamous neoplasia with topical 1% 5-fluorouracil

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ABSTRACT

Ocular surface squamous neoplasia (OSSN) is the most common type of ocular tumour. An eighty-year-old man with an elevated lesion in the right eye was diagnosed to have OSSN. 1% topical 5-FU was started as an intermittent treatment. Examination during each visit showed consistent reduction in size of lesion. The patient showed complete regression with no recurrence following treatment with 1% 5-FU at 3 months from presentation. Topical treatment with 1% 5-FU provides excellent prognosis in cases of OSSN.

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1. Introduction

Ocular surface squamous neoplasia (OSSN) being the most common type of ocular tumour, is still rare with a low incidence of 8.4 per million people per year.¹ It comprises a spectrum of epithelial squamous conditions ranging from dysplasia and carcinoma insitu to invasive carcinoma.² Previous history of OSSN, ultraviolet light exposure, prior skin cancer, older age and male gender are considered as the strongest risk factors for OSSN.³ Weakly associated risk factors include human immunodeficiency virus (HIV), human papilloma virus (HPV), and smoking.⁴

The gold standard of treatment for OSSN was surgical excision using a no-touch technique with adjuvant alcohol and cryotherapy. Nowadays, medical management by topical chemotherapeutic agents like interferon alfa-2b (IFN), 5-fluorouracil (5FU), and mitomycin C (MMC) as primary therapy for OSSN is in trend.⁵

Surgical excision provides rapid cure of lesions and it is both, diagnostic and therapeutic. But the recurrence rate is as high as 56% because subclinical microscopic disease is not being treated.³ Also, limbal stem cell deficiency is a complication following excision.

Topical chemotherapeutic agents treat the entire ocular surface, which is very helpful in treating microscopic subclinical disease.⁵ However, longer time is taken for resolution and patient compliance is low.

2. Case Report

An 80-year-old man presented with a lesion in the right eye for 2 months which was insidious in onset, gradually progressive, painless, and not associated with diminution of vision. On slit lamp evaluation, an elevated, nodular lesion was found on medial side extending from 11 O'clock to 5 O'clock position, encroaching 4mm of the corneal surface, measuring 9mm horizontally and 11mm vertically. (Figure 1a) Senile immature cataract was noted in the right eye whereas left eye was pseudophakic. HR-OCT showed hyper reflectivity and abrupt transition from normal to

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abnormal tissue (Figure 2). A provisional diagnosis of OSSN was made with a differential diagnosis of squamous papilloma. Impression cytology was performed to confirm OSSN and to document dysplasia (Figures 3 and 4). Excision biopsy was planned, but as the lesion was large, reduction in size of the lesion using topical therapy was considered prior to surgery.

1% topical 5-FU was started four times per day for 1 week which showed decrease in size of the lesion. Hence, patient was planned for further cycles of 5-FU. It was followed by 3 weeks of drug free interval. 2 more similar cycles of therapy were given. The patient presented with symptoms of toxicity like burning sensation, watering in the eye which was treated with preservative free lubricants during the interval period. Conjunctival biopsy, 5 mm in size, was taken adjacent to nasal limbus and sent for histopathologic examination.

3. Results

Patient examination during each visit showed consistent reduction in size of lesion (Figure 1). At 3 months post treatment follow up, no recurrence of lesion was noted on clinical evaluation (Figure 1a) or histopathologic examination and showed a good resolution on HR-OCT (Figure 5).

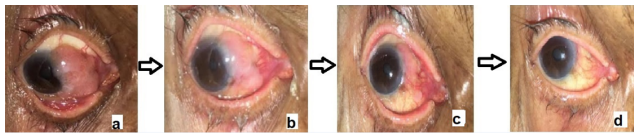


Fig. 1: Clinical photo Reduction in size of lesion following cycle 1 of 1% 5-FU Further reduction in size of lesion following cycle 2 of 1% 5-FU Final result as resolution of lesion at 3 months follow-up



Fig. 2: HR-OCT image of OSSN

4. Discussion

OSSN lesions range from simple dysplasia to invasive squamous cell carcinoma. OSSN can involve cornea, conjunctiva and limbus.² Although clinical appearance is typical, histopathology serves as the gold standard for diagnosis. HR-OCT shows hyperreflective, thickened epithelium with an abrupt transition between normal and cancerous epithelium.

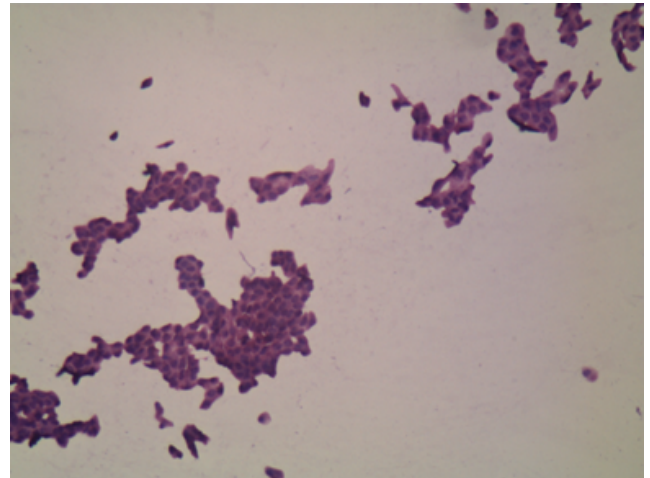


Fig. 3: Microphotograph of impression cytology showing dysplastic conjunctival epithelial cells (H&E stain 100x)

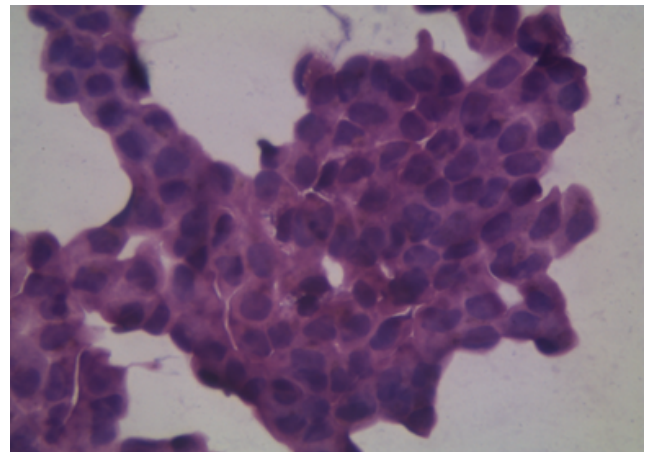


Fig. 4: High power of dysplastic conjunctival epithelial cells showing lost polarity and high Nuclear cytoplasmic ratio (H&E stain 400x)

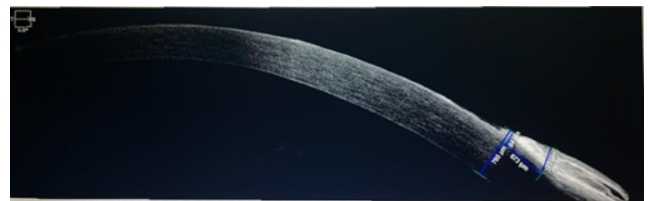


Fig. 5: HR-OCT image at 3 month follow up

The treatment of choice for OSSN is surgical excision with no-touch technique and base cryotherapy but has the disadvantages of iatrogenic limbal stem cell deficiency (LSCD) and high chance of recurrences (33%).⁶

Topical chemotherapy use is advocated mostly as a means of debulking prior to excision as neo adjuvant therapy. But, in our study it was used as the sole treatment. Topical chemotherapeutic agents reduce the risk of recurrence (7.3% in a study by Parrozzani et al where 5-FU was used) as they spread all over the ocular surface and kill the neoplastic cells which are invisible to the naked eye. It also has lesser risk of LSCD and lower cost.⁷ Agents available are 5-FU, interferon alpha-2b (IFN-2b), or mitomycin C (MMC).^{8,9} Our study used topical 5-FU because of its advantages over surgical treatment and other topical chemotherapeutic agents. In 1986, topical 5FU was first used for treating premalignant lesions of the eyelid, cornea, conjunctiva. Thereafter, studies have reported 5-FU with a high frequency of resolution.¹⁰

IFN being an endogenous protein with antiviral and antineoplastic properties has a better side effect profile. Advantages of 5-FU include shorter duration of treatment than with IFN, it does not need any refrigeration like in IFN as solutions of 5-FU are stable for weeks at 25°C, it is less expensive than other agents, and patients prefer the 1 week per month treatment than the daily administration needed in IFN.

MMC being a potent antimetabolite causes pain in most patients and rarely, corneal and scleral melts.⁸ 5-FU is a structural analog of thymine which inhibits DNA formation by blocking the enzyme thymidylate synthetase. Tumour cells which are rapidly multiplying cells require more DNA and RNA than normal cells, thus taking up higher amounts of 5-FU, allowing selective targeting of cancerous lesions.¹⁰ Therefore, 5-FU is not as toxic as MMC.

Treatment course of topical 5-FU ranges from a long course of four times daily for a month followed by 3-month off treatment to a short course of four times daily for 4–7days, followed by 3-week off treatment until resolution of OSSN.⁷ We followed the short course to which patient responded well.

Hyperaemia, pain, irritation, watering of eyes and photo sensitivity are the common side effects.⁸ Higher doses than recommended cause ocular surface toxicity and corneal melting, managed by stopping the drug, use of non-preserved lubricants, eye patching, systemic doxycycline, and topical steroids. Our patient also developed symptoms of surface toxicity in the form of burning sensation in the eye following second cycle which was successfully managed by lubricant eye drops.

A series by Parrozzani et al included 41 patients, of whom 22 were treated primarily with 5-FU 4 times daily for 1 month. All tumours resolved completely after mean of 1.9 monthly cycles. However, 3 patients (7.3%) demonstrated early recurrence.⁷

5. Conclusion

Topical 1% 5-FU successfully treats OSSN and can be used as a preferred chemotherapeutic agent instead of surgical excision. HR-OCT is an excellent non-invasive adjuvant tool in diagnosis of OSSN.

6. Conflict of Interest

The authors declare no relevant conflict of interest with respect to research, authorship and or publication of this article.

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