Case Report

Neoadjuvant Topical Mitomycin C for an Extensive Ocular Surface Squamous Neoplasia

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Abstract

A sixty-five-year old male presented with an enlarging mass over the ocular surface involving nasal area of conjunctiva, superior and inferior fornix and covering the corneal surface obscuring pupil barring a temporal island of cornea. On the basis of clinical features and impression cytology, the diagnosis of ocular surface squamous neoplasia (OSSN) was made and patient was given neoadjuvant chemotherapy in the form of topical mitomycin C (0.04%) for 6 cycles. Excision biopsy with cryotherapy and amniotic membrane transplantation was performed. At the last follow-up, patient showed no clinical evidence of OSSN.

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Keywords: *Ocular surface squamous neoplasia (OSSN); mitomycin C (MMC); neoadjuvant chemotherapy; chemoreduction*

Introduction

Ocular surface squamous neoplasia (OSSN) term encompasses the various dysplastic lesion of conjunctiva and cornea which include squamous papilloma, conjunctival intraepithelial neoplasia (CIN), carcinoma in-situ (CIS), invasive squamous cell carcinoma.[1] Advanced age, exposure to UV light, human papilloma virus (HPV) infection, xeroderma pigmentosum, chronic irritants, immunosuppression, and human immunodefficiency virus (HIV) infection are the various risk factors associated with this disease. It presents in the interpalpebral region of the perilimbal conjunctiva and extends over the corneal surface. The management of OSSN poses a significant challenge to an ophthalmic surgeon. Various treatment modalities like complete excision with 4 mm clear margins, amniotic membrane transplantation, use of intraoperative mitomycin-C (MMC), topical chemotherapy (MMC, interferon α2b, 5-fluorouracil) cryotherapy, enucleation, exenteration, and radiotherapy have been described in the literature.[2-6] However very few reports describe the use of neoadjuvant chemotherapy in the form of topical MMC.[7,8] Herein we report a unique case of an extensive OSSN which was managed successfully with preoperative topical mitomycin-C followed by excision with amniotic membrane transplantation and cryotherapy.

Report of case

A sixty-five-year old male presented to the out-patient services of Ophthalmology department of a rural based tertiary care hospital with the complaints of enlarging painless mass over the conjunctiva and cornea of the right eye. He first noticed the mass 5 years before presentation which was gradually increasing in size and extent. It was associated with gradual diminution of vision and watering in the right eye. There were no complaints in the left eye. On diffuse light examination, the mass was lying over the nasal conjunctiva involving superior and inferior forniceal conjunctiva and almost 2/3rd of cornea barring temporal island of uninvolved cornea. The mass was reddish in color due the coiled, spiral and tortuous conjunctival vascularization with feeder vessel. The mass was painless, soft to firm in consistency with restricted mobility. The pupil was also obscured by the overlying mass over the cornea and therefore was not visible [Figure 1A]. Ultrasound

Figure 1: *Clinical photographs of a patient with ocular surface squamous neoplasia at presentation (A); six-weeks post neoadjuvant chemotherapy [topical mitomycin C (0.04%)] (B); six-months after the excision with cryotherapy, and amniotic membrane transplantation (C).*

biomicroscopy ruled out the further extension of tumor mass into anterior segment, sclera, and ciliary body. Based on American Joint Committee on Cancer (AJCC) staging on ocular surface squamous neoplasia, tumor was staged as T3 category due to the size >5 mm with involvement of forniceal conjunctiva.[9]

Patient uncorrected visual acuity was hand movement close to face in the right eye and 20/200 in the left eye. Rest of the details like anterior chamber, lens status, fundus examination could not be performed in the right eye due to the non-visualization by overlying mass. The ocular examination in the left eye showed cataract and rest was with-in-normal limits. USG-B scan showed no abnormality in lens status, vitreous cavity and retina. On the basis of clinical features the diagnosis of ocular surface squamous neoplasia (OSSN) right eye was made which was confirmed with impression cytology. Scrape smears prepared from the conjunctival lesion were cellular and showed several clusters and sheets of malignant squamous cells showing marked nuclear pleomorphism, nuclear overlapping, prominent nucleoli and frequent mitoses [Figure 2A]. Based on these features diagnosis of squamous cell carcinoma was made. Testing for HIV was negative.

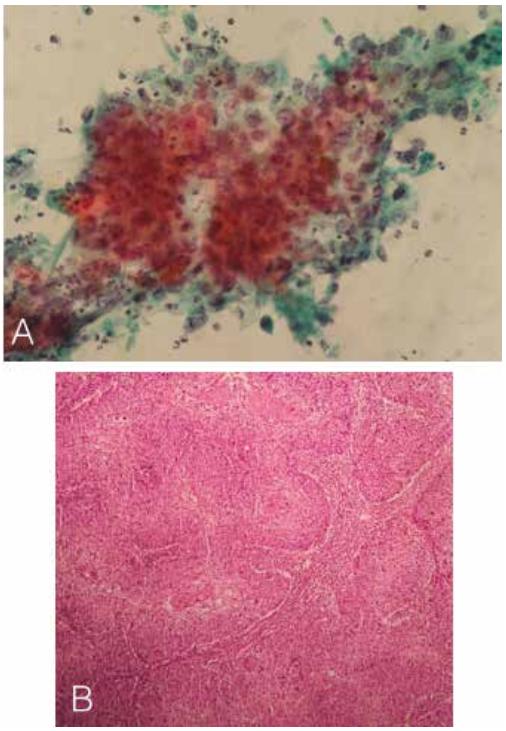

Figure 2: *Histopathological micrographs of the lesion. (A) Scrape smear showing sheet of ma-lignant squamous cells displaying marked pleomorphism, nuclear overlapping and prominent nu-cleoli (Pap stain 400X); (B) Histological section showing infiltrating squamous cell carcinoma (H/E 100X).*

Patient was started preoperative chemotherapy in the form of topical mitomycin-C (0.04%) QID for 4 days a week. Six cycles of chemotherapy were given. After 6 weeks, the lesion was less vascularized and was retracted nasally leaving temporal area more clearer so that the pupil was visible [Figure 1B]. Excision biopsy, superficial sclerectomy, and absolute alcohol application for superficial corneal debridement with amniotic membrane transplantation was performed successfully. Cryotherapy was performed over the margins of conjunctival tissue bordering the area of excised lesion. On postoperative assessment, patient was having corneal and conjunctival epithelial defect which resolved gradually in 2 weeks. The visual axis was clear and pupil was well reactive. Patient gained a vision of 20/200 in the right eye with cataract explaining the further diminution of vision. On his last follow-up (6 months), patient maintained the vision and no clinical evidence of OSSN was found [Figure 1C]. The diagnosis of OSSN was further confirmed on histopathological examination of the excised lesion [Figure 2B].

Discussion

The management of OSSN took a huge leap from just a simple excision to a combination of therapy including use of preoperative, intraoperative or postoperative topical chemotherapy.[5] Topical chemotherapy either in the form of monotherapy or combination therapy has found to be an effective treatment in earlier studies.[3-8] The prognosis of OSSN has really improved after using the chemotherapy as the recurrence rate is minimized. Use of adjuvant postoperative topical chemotherapy has been shown to be an effective strategy to minimize the recurrence rate.[4]

Chemoreduction prior to surgery has gained importance in the management of many tumors including retinoblastoma.[10] Singh et al reported the successful use of neoadjuvant MMC in the treatment of conjunctival and corneal intraepithelial neoplasia.[7] Chemoreduction with topical MMC prior to excision of extensive OSSN has been reported by Shields et al.[8] In their series, topical MMC was effective in reducing the tumor base a mean of 57% using a mean of 4 cycles. In our case the tumor was involving superior fornix to inferior fornix and medially canthus, and more than 95% of corneal surface without intraocular invasion. In such an extensive involvement, it was unlikely to have a complete response with topical MMC alone therefore topical MMC (0.04%) was used as a neoadjuvant chemotherapy to allow the chemoreduction prior to excision of tumor so that the conjunctival resection could be minimized and reducing the chances of recurrence. After 4 cycles of MMC tumor showed some regression on the corneal side making pupil visible. Amniotic membrane transplantation was performed to cover the large defect.

Topical MMC is associated with multiple toxic effects like corneal melting, scleral necrosis, uveitis, erythema, and punctual stenosis.[11] Interferon alpha 2b (IFN α2b) has also been found to be an effective treatment option for the management of OSSN for immunoreduction (to reduce tumor size), immunotherapy (as a sole treatment for tumor regression), or immunoprevention (to prevent tumor recurrence) in a retrospective series of 30 patients.[12] Topical IFN α2b was used in the dosage of 1 MIU/cc 4 times per day with additional perilesional IFN α2b 95 MIU/cc once a month for conjunctival or conjunctivocorneal lesions. Its use has been reserved for extensive tumor, lesion limited to corneal surface, and recurrent tumor post surgical excision and/or MMC.[12] However, cost is the major limiting factor

for IFN α2b. Our patient did not have any of the side effect associated with MMC. Though rare, OSSN lesion has propensity to involve anterior segment which may present as granulomatous iridocyclitis as reported in a series of 5 patients by Shields et al.[13] This case report highlights an important role of neoadjuvant topical chemotherapy (MMC 0.04%) prior to the excision of an extensive OSSN with amniotic membrane transplantation and cryotherapy. Topical MMC is an effective treatment for extensive OSSN.

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