Neoadjuvant chemotherapy for invasive squamous cell carcinoma of the conjunctiva: A case report

Akshay Gopinathan Nair, Swathi Kaliki, Dilip Kumar Mishra[1], Vijay Anand Reddy, Milind N Naik

A 40-year-old male presented with an orbital extension of conjunctival squamous cell carcinoma (SCC). The orbital mass was seen protruding outward from the left palpebral fissure overhanging the lower eyelid, completely obscuring the globe and lower lid. The patient gave a history of excision biopsy, which was histopathologically diagnosed as ocular surface squamous neoplasia. He also gave a history of tumor recurrence, which gradually progressed to assume the form of the presently visible orbital mass. Computed tomography of the orbits showed the mass extending into the left orbit causing superior displacement of the globe. After a negative locoregional and systemic metastatic screening, neoadjuvant intravenous systemic chemotherapy with cisplatin and 5-fluorouracil were initiated in an attempt to reduce the size of the tumor. Three cycles of tri-weekly chemotherapy resulted in a significant reduction of the orbital tumor size with the globe and the lower lid being visible, thus making a lid-sparing orbital exenteration possible. The patient subsequently underwent an orbital exenteration and at 6-month follow-up, the patient was free from local and regional disease. To our knowledge, this is the first reported case where systemic neoadjuvant chemotherapy has been used to reduce the size of invasive SCC with orbital extension, thereby permitting a lid-sparing orbital exenteration.

Key words: Chemotherapy, conjunctiva, exenteration, eye, neoadjuvant, ocular surface squamous neoplasia, squamous cell carcinoma, tumor

"Ocular surface squamous neoplasia" (OSSN) represents a spectrum of diseases ranging from simple dysplasia to carcinoma *in situ* to invasive squamous cell carcinoma (SCC) that involves the conjunctiva, limbus, and/or cornea.[1] The treatment of OSSN depends on the tumor size and tumor extension. Topical mitomycin-C (MMC), interferon alpha-2b, and 5-fluorouracil (5-FU) have been used extensively for chemoreduction and/or as the sole treatment for noninvasive OSSN.[2-4] The treatment of choice for noninvasive OSSN continues to remain wide surgical excision of the conjunctival lesion by "no touch" technique with adjunctive double freeze-thaw cryotherapy to the surgical margins and alcohol-assisted kerato-epitheliectomy for corneal involvement.[4] Plaque radiotherapy is indicated in scleral-invasive SCC, whereas external beam radiation therapy has also been reported to be useful in the treatment of recalcitrant SCC of the conjunctiva.[5,6]

The eyes with intraocular invasion of conjunctival SCC are enucleated and in those with orbital invasion, orbital exenteration is required.[6,7] Since orbital extension of conjunctival SCC is relatively rare, no study has evaluated the role of systemic chemotherapy in its management. We present a case of conjunctival SCC with orbital extension, with no metastatic disease, which was treated by intravenous neoadjuvant chemotherapy (NAC) (cisplatin and 5-FU) followed by an eyelid-sparing orbital exenteration. Chemotherapy resulted in significant reduction in tumor volume, facilitating an eyelid-sparing orbital exenteration.

Case Report

A 40-year-old male presented to us with a pink, fleshy mass protruding from the left palpebral fissure overhanging the lower lid, completely obscuring the left globe. Best-corrected visual acuity (BCVA) was 20/20 N6 in the right eye; however, vision could not be recorded in the left eye. There was a significant history of white nodular growth over the left ocular surface 3 years ago, which gradually and painlessly increased in size. He had undergone excision biopsy of the conjunctival lesion with an amniotic membrane grafting elsewhere 1 year ago. Details of the use of intraoperative MMC or cryotherapy were unavailable. Histopathology reports confirmed the diagnosis of SCC of the conjunctiva. The details regarding the status of tumor margins and tumor base were not available. The patient was advised to use topical MMC in the left eye (OS). However, the patient did not use any topical or systemic medication postoperatively. Over the past year, he reported a recurrence of the nodule in the left eye with rapid increase in its size, which subsequently obscured the entire left eye and presented to us with an orbital mass [Fig. 1a]. The examination of the anterior and posterior segments of the right eye (OD) was within normal limits. BCVA OD was 20/20. A pink, fleshy mass measuring 5 cm × 3 cm × 3 cm was visible over the left ocular surface obscuring the view of the left eye. The posterior limit of the mass was not palpable. No regional lymph nodes were palpable. A clinical diagnosis of

Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/0301-4738.176026

The Operation Eyesight Universal Institute for Eye Cancer, L V Prasad Eye Institute, [1]Department of Ophthalmic Pathology (DKM), L V Prasad Eye Institute, Hyderabad, Telangana, India

Correspondence to: Dr. Swathi Kaliki, The Operation Eyesight Universal Institute for Eye Cancer, L V Prasad Eye Institute, Banjara Hills Road No. 2, Hyderabad - 500 035; Telangana. E-mail: Indiakalikiswathi@yahoo.com

Manuscript received: 19.04.15; Revision accepted: 13.11.15

Cite this article as: Nair AG, Kaliki S, Mishra DK, Reddy VA, Naik MN. Neoadjuvant chemotherapy for invasive squamous cell carcinoma of the conjunctiva: A case report. Indian J Ophthalmol 2015;63:927-9.

conjunctival SCC with orbital extension was made. Computed tomography of the orbits showed a well-defined, homogenous, isodense mass over the left eye extending into the inferior orbit, indenting the globe, and displacing [Fig. 1b]. There was no evidence of bony erosion or tumor invasion into the paranasal sinuses. Incisional biopsy confirmed the diagnosis of conjunctival SCC. Owing to the large tumor size and inferior extent of the tumor, an eyelid-sparing orbital exenteration with tumor-free margins at that juncture was not feasible. A thorough systemic evaluation showed no metastatic disease. The systemic evaluation included a chest X-ray, ultrasound examination of the abdomen, liver, and renal function tests. Subsequently, NAC was planned with an aim to reduce the tumor size to facilitate an eyelid-sparing orbital exenteration.

The patient received three cycles of intravenous chemotherapy (cisplatin 150 mg and 5-FU 1000 mg daily for 3 days during each cycle) with each cycle being repeated at intervals of 3 weeks. After each cycle of chemotherapy, a reduction in the size of the orbital component of the tumor was noted [Fig. 1c and d]. Throughout the chemotherapy cycles, all hematological parameters were stable, and no serious adverse effects were observed. After the third cycle, the left globe was visualized in an elevated and abducted position owing to the tumor invasion of the extraocular muscles [Fig. 1e]. There was gross ectropion of the left lower lid with complete tarsal show. There was evidence of OS diffuse SCC involving the entire conjunctival surface and cornea. The BCVA OS was recorded as 20/40. The significant reduction in tumor size [Fig. 1f] made an eyelid-sparing orbital exenteration possible; which the patient underwent 2 weeks after the last cycle of chemotherapy. The histopathological examination of the exenterated specimen showed a tumor mass involving the limbus, conjunctiva, parts of the cornea, and infiltrating into the adjacent orbital tissue. The lesion showed large sheets of cells with abundant cytoplasm, large vesicular nucleus, and prominent nucleoli [Fig. 2a]. Bizarre tumor giant cells and squamous differentiation were noted, confirming the diagnosis of invasive SCC [Fig. 2b]. There was no evidence of intraocular tumor invasion, perineural invasion, and the orbital tissue margins were clear of tumor. At last follow-up of 6 months, the socket had healed well with no local or regional tumor recurrence.

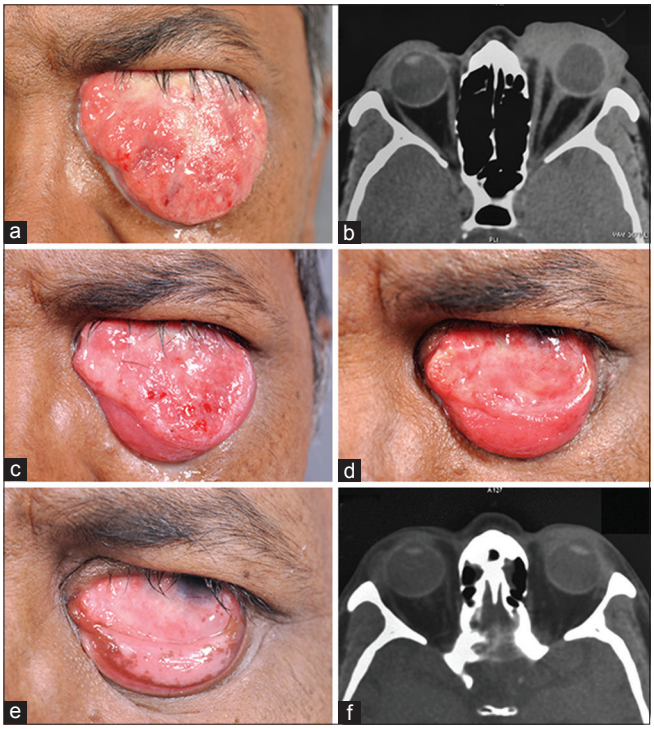

Figure 1: Response of conjunctival squamous cell carcinoma to systemic neoadjuvant intravenous chemotherapy. (a) Clinical photograph showing a pink, fleshy, mass protruding from the left palpebral fissure overhanging the lower lid completely obscuring the globe. (b) Computed tomography scan – axial cut through the orbit showing the isodense mass lesion surrounding the left globe. (c) Clinical photograph showing reduction in the tumor size after one cycle of chemotherapy. (d) Clinical photograph showing further reduction in the tumor size after two cycles of chemotherapy. (e) Preoperative clinical photograph showing marked reduction in the tumor size after the third cycle of chemotherapy. The globe is in an elevated and abducted position owing to the tumor invading the extraocular muscles. There is evidence of diffuse conjunctival squamous cell carcinoma. Severe ectropion of the lower lid with complete tarsal show is also noted. (f) Computed tomography scan after three cycles of chemotherapy demonstrating a radiologically evident reduction in the size of the tumor around the left eye

Discussion

The treatment of choice for conjunctival SCC with orbital invasion is orbital exenteration. Orbital exenteration is a disfiguring surgery, which is performed mainly to achieve surgical cure for orbital malignancies or for ocular/periocular tumors with orbital extension. Based on the extent of orbital tissue removal, orbital exenteration can be divided into three categories: Subtotal, total, and extended exenteration. Based on the eyelid status, exenteration can be classified as eyelid-sparing exenteration and eyelid-sacrificing exenteration. Eyelid-sparing exenteration is a form of subtotal exenteration.[8,9] An eyelid-sparing exenteration heals faster since primary wound closure is achieved and is cosmetically acceptable compared to eyelid-sacrificing exenteration.

Intravenous NAC has been used to shrink large tumors and make them amenable to surgical resection.[10,11] Cisplatin

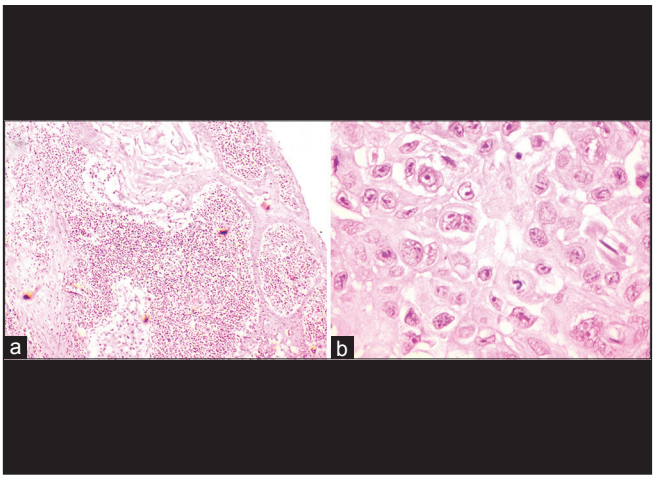

Figure 2: Histopathology of exenterated specimen. (a) Photomicrograph showing conjunctival epithelium superficially and below are large sheets of cells with abundant cytoplasm, large vesicular nuclei with prominent nucleoli (H and E, ×10). (b) Photomicrograph showing hyperchromatic nucleus and bizarre tumor giant cells (H and E, ×40)

and 5-FU have been used at the prescribed dosage as NAC in primary and metastatic head and neck malignancies.[12,13] These two drugs do not have overlapping toxicities, thus making it an effective combination therapy.[12] Cisplatin and 5-FU have been used in combination in advanced locoregional and metastatic SCC of the skin and as a part of neo-adjuvant chemotherapy regimes in periocular and intraocular malignancies.[14-17] Therefore, given their established safety profile and anecdotal successful reports in ophthalmology, these drugs were used in the Institutional Review Board-approved protocol-based NAC regime in our patient. Based on literature review, the use of NAC for conjunctival SCC has not been reported.

Our patient, on presentation, had an orbital mass, which was causing a mechanical ectropion of the lower lid and completely obscuring it. The aim of the NAC was to reduce the tumor size such that a lid-sparing exenteration could be performed. In the absence of systemic metastasis, surgical cure from the disease would have been possible only with an eyelid-sacrificing orbital exenteration. While it did not change the surgery of choice – orbital exenteration – the use of NAC in this patient showed a remarkable reduction in tumor size making eyelid-sparing orbital exenteration possible with tumor-free surgical margins.

Eyelid-sparing exenteration is a less mutilating surgery with quicker recovery, lesser complications, lower postoperative morbidity, and good cosmetic outcomes by the way of facilitating the use of glued-on orbital exenteration prosthesis.[15,18]

Although larger studies with more number of cases are required to validate the role of systemic NAC in the management of conjunctival SCC with orbital extension, our case demonstrates that NAC may be useful in chemoreduction of the tumor prior to surgery in advanced cases of OSSN without regional or systemic metastasis.

Financial support and sponsorship

Support provided by Hyderabad Eye Research Foundation, Hyderabad. The funders had no role in the design and conduct of the study, in the collection, analysis, and interpretation of the data, and in the preparation, review, or approval of the manuscript. Swathi Kaliki, M.D., has had full access to all the data in the study and takes responsibility for the integrity and accuracy of the data.

Conflicts of interest

There are no conflicts of interest.

References

1. Lee GA, Hirst LW. Ocular surface squamous neoplasia. Surv Ophthalmol 1995;39:429-50.
2. Basti S, Macsai MS. Ocular surface squamous neoplasia: A review. Cornea 2003;22:687-704.
3. Rudkin AK, Muecke JS. Adjuvant 5-fluorouracil in the treatment of localised ocular surface squamous neoplasia. Br J Ophthalmol 2011;95:947-50.
4. Nanji AA, Sayyad FE, Karp CL. Topical chemotherapy for ocular surface squamous neoplasia. Curr Opin Ophthalmol 2013;24:336-42.
5. Graue GF, Tena LB, Finger PT. Electron beam radiation for conjunctival squamous carcinoma. Ophthal Plast Reconstr Surg 2011;27:277-81.
6. Shields JA, Shields CL, De Potter P. Surgical management of conjunctival tumors. The 1994 Lynn B. McMahan lecture. Arch Ophthalmol 1997;115:808-15.
7. Arepalli S, Kaliki S, Shields CL, Emrich J, Komarnicky L, Shields JA. Plaque radiotherapy in the management of scleral-invasive conjunctival squamous cell carcinoma: An analysis of 15 eyes. JAMA Ophthalmol 2014;132:691-6.
8. Pe'er J, Frucht-Pery J. Ocular surface squamous neoplasia. In: Singh AD, Damato BE, Pe'er J, Murphree AL, Perry JD, editors. Clinical Ophthalmic Oncology. 1st ed. Philadelphia, PA: Mosby Elsevier; 2007. p. 136-40.
9. Ben Simon GJ, Schwarcz RM, Douglas R, Fiaschetti D, McCann JD, Goldberg RA. Orbital exenteration: One size does not fit all. Am J Ophthalmol 2005;139:11-7.
10. Yeatts RP. The esthetics of orbital exenteration. Am J Ophthalmol 2005;139:152-3.
11. Cho JH, Park JM, Park HS, Park S, Kim SI, Park BW. Oncologic safety of breast-conserving surgery compared to mastectomy in patients receiving neoadjuvant chemotherapy for locally advanced breast cancer. J Surg Oncol 2013;108:531-6.
12. Pendleton KP, Grandis JR. Cisplatin-based chemotherapy options for recurrent and/or metastatic squamous cell cancer of the head and neck. Clin Med Insights Ther 2013;5:103-16.
13. Khansur T, Allred C, Little D, Anand V. Cisplatin and 5-fluorouracil for metastatic squamous cell carcinoma from unknown primary. Cancer Invest 1995;13:263-6.
14. Khansur T, Kennedy A. Cisplatin and 5-fluorouracil for advanced locoregional and metastatic squamous cell carcinoma of the skin. Cancer 1991;67:2030-2.
15. Murthy R, Honavar SG, Burman S, Vemuganti GK, Naik MN, Reddy VA. Neoadjuvant chemotherapy in the management of sebaceous gland carcinoma of the eyelid with regional lymph node metastasis. Ophthal Plast Reconstr Surg 2005;21:307-9.
16. Priyadarshini O, Biswas G, Biswas S, Padhi R, Rath S. Neoadjuvant chemotherapy in recurrent sebaceous carcinoma of eyelid with orbital invasion and regional lymphadenopathy. Ophthal Plast Reconstr Surg 2010;26:366-8.
17. Gogia A, Pushker N, Sen S, Bakhshi S. Avoidance of exenteration in orbital sebaceous gland carcinoma with neoadjuvant chemotherapy. Graefes Arch Clin Exp Ophthalmol 2013;251:2479-80.
18. Shields JA, Shields CL, Demirci H, Honavar SG, Singh AD. Experience with eyelid-sparing orbital exenteration: The 2000 Tullos O. Coston Lecture. Ophthal Plast Reconstr Surg 2001;17:355-61.