

Plaque Radiotherapy in Recurrent or Incomplete- Excised Conjunctival Squamous Cell Carcinoma and Melanoma

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Abstract

Purpose: To assess the results of brachytherapy in patients with recurrent or incomplete excised conjunctival squamous cell carcinoma (SCC) and malignant melanoma.

Methods: Three patients underwent brachytherapy of one eye and one patient underwent brachytherapy of both eyes with ruthenium-106 (RU-106) plaques, all of them had a history of incomplete resection or recurrence of the tumor after surgery. All patients were male with an average age at diagnosis of 54 years (range, 34-76 years). The shape and the size of plaques were determined based on location and size of the suspected area. The plaque was inserted to deliver a target dose of 80-100 Gy in the region of conjunctival malignancy. The diagnosis was squamous cell carcinoma in three eyes and conjunctival melanoma in two eyes. All patients had surgical history of one to three previous excisions with or without cryotherapy before brachytherapy. There were microscopic residual tumors after excision in 2 eyes and recurrent lesion was evident in 3 other eyes. A mean dose of 95 Gy was delivered to the tumor bed.

Results: Complete tumor regression without any evidence of recurrent lesion was obtained in all five eyes. The patients were followed for 32 months on average (range, 18-42 months). No radiation related complication was detected, with an exception of a dry eye in the last follow up.

Conclusion: Brachytherapy with RU-106 plaque is an alternative method for treatment of selected patients with recurrent or residual conjunctival SCC and melanoma.

Keywords: Brachytherapy, Ruthenium-106 Plaque, Conjunctival Squamous Cell Carcinoma, Conjunctival Melanoma

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Introduction

Ocular Surface Squamous Neoplasia (OSSN) and malignant melanoma are common conjunctival corneal malignancies. OSSN is the most frequent malignancy of conjunctiva

including dysplasia or mild conjunctival intraepithelial neoplasia (CIN), carcinoma *in situ* or severe CIN and invasive conjunctival squamous cell carcinoma.^{1,2,3}

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Different therapeutic options have been described in management of ocular surface tumors; however, the mainstay of treatment of conjunctival tumors is the complete excision of these lesions.⁴ Due to high tendency of these tumors to recur after excision, many authors believe that simple excision of the lesion is inadequate.²⁻⁴ Therefore, wide excision of lesions with adjuvant cryotherapy of tumor-free conjunctival margins and/or scleral base of the tumor with double freeze-thaw technique are the most widely suggested methods.^{5,6} The recurrence rate following OSSN excision has been reported to be between 15–52% with an average of 30%.⁷ The recurrence rate is mostly related to how successfully total resection of tumor is done. Subsequently, 53% of incomplete resected lesions recur while less than 5% of tumors with clear microscopic margins show future recurrences.⁸

A wide range of recurrence rate of conjunctival melanoma has been attributed to partial excision and follow-up period. The local recurrence rate at five years and 10 years have been reported to be between 5-26% and 42-51%, respectively.^{9,10}

Recurrent lesions are associated with a poor prognosis and tendencies to metastasize to brain, regional lymph nodes and other organs.¹¹ In spite of the combined use of excision and cryotherapy, high recurrence rate of OSSN and conjunctival melanoma has been reported.¹⁸ Therefore, several adjuvant therapies, are being investigated including brachytherapy (plaque radiotherapy) with different sources like strontium-90¹², ruthenium-106 (RU-106)¹³ and topical chemotherapy agents like Mitomycin-C (MMC),^{14,15} 5-Fluorouracil¹⁶ and Interferon- α .^{17,18}

Herein, we report the short-term results of treatment with RU-106 radioactive plaque on five eyes of four patients with histopathologically confirmed recurrent or incomplete excised conjunctival squamous cell carcinoma and melanoma.

Methods

All patients were male and the mean age at diagnosis was 54 years (range, 34–76 years).

Case 1

A 76-year-old man with history of redness and foreign body sensation and enlarging bulbar

conjunctival mass on temporal part of his right eye was diagnosed to have a conjunctival melanoma by a general ophthalmologist. Because of recognized microscopic involvement of margins after excisional biopsy, the patient was referred for plaque radiotherapy. He was treated with RU-106 plaque with a target dose of 93 Gy.

Case 2

A 36-year-old man underwent excisional biopsy combined with cryotherapy of tumor-free conjunctival margins. Histopathologic findings were compatible with diagnosis of conjunctival melanoma with free margins. The patient required another excisional biopsy for recurrent lesion after seven years. Because of deep penetration of tumor, plaque radiotherapy with calculated dose of 101 Gy was performed for residual tumor.

Case 3

A 34-year-old man with possible diagnosis of an enlarging melanotic nevus during the last two to three months was scheduled for excisional biopsy with cryopexy. Histopathologic assessment of the specimen confirmed the diagnosis of squamous cell carcinoma with unclear margins. The patient was referred to oncology service and treated with RU-106 plaque for a target dose of 80 Gy.

Case 4

A 70-year-old man with history of recurrent conjunctival OSSN conjunctival multiple excisional biopsy and chemotherapy with MMC during the last seven years underwent plaque radiotherapy due to recent recurrent conjunctival SCC at suprotemporal quadrant.

We treated the tumor with 93 Gy of radiation for scleral bed of the lesion. Eighteen months following the first application of RU-106 plaque, the patient developed another recurrent lesion in nasal side, separate from the field of brachytherapy.

Histopathologic assessment of map biopsy showed the presence of severe CIN. We discussed the situation with patient and he decided to undergo plaque radiotherapy instead of topical chemotherapy with MMC. Brachytherapy with a target dose of 83 Gy was done for the bed of new recurrence.

Five eyes of four patients were selected for RU-106 plaque radiotherapy. A complete ophthalmic examination including the best

corrected visual acuity (BCVA) assessment, intraocular pressure measurement (IOP), and anterior segment and fundus examination were done for each patient.

Clinical records were collected regarding demographic data of patients, tumor features and radiation variables. Pathologic proven diagnosis was conjunctival SCC in three eyes and malignant melanoma in two eyes. Concurrent ocular abnormalities in the affected eye included operculated hole (one eye), pseudophakia (one eye) and cataract (one eye).

Microscopic or macroscopic evidence of residual tumor after surgical resection and recurrent tumor mass were present in three and two eyes, respectively.

A RU-106 plaque (Bebig Company, Germany) was sutured to the sclera (Figure 1) to deliver approximately 80–100 Gy radiation with 2 mm tissue penetration to the target area of residual tumor. Temporary blepharorrhaphy was done right after plaque insertion. The plaque was removed when the calculated dose had been delivered.



Figure 1. Ruthenium-106 plaque has been sutured to sclera on the suspected area.

Results

We treated five eyes of four patients (having recurrent or incomplete-excised conjunctival tumors) with RU-106 plaque radiotherapy at the oncology service at Rassoul Akram Hospital.

All tumors had previously been treated elsewhere with single or multiple excisional biopsies with or without cryotherapy prior to referral. The BCVA was $20/20$ in two patients, $20/25$ in one patient and $20/30$ in one patient. No

patient developed significant visual loss (more than one line of Snellen chart) in the last visit. The average follow-up time was 32 months (range, 18–42 months). None of patients experienced tumor recurrence or radiation related complications during follow-up sessions except to a mild dry eye in one patient. All systemic work-up and laboratory examinations have been within normal limits so far. The mean delivered dose of radiation was 95 Gy (range, 83–106 Gy).

Case 1

No evidence of recurrence was detected through 18 months after plaque radiotherapy.

Case 2

No recurrent lesion has been observed after 36 months.

Case 3

There was no recurrent tumor in 32 months following brachytherapy.

Case 4

We successfully treated the recurrent conjunctival SCC at suprotemporal quadrant. The other recurrent location in nasal side which was developed 18 months later is free of tumor within 24 months after second plaque radiotherapy.

Discussion

Based on preliminary results of our study, plaque radiotherapy appears to be a reasonable alternative to more extensive and invasive surgery in selected cases of recurrent or incomplete excised conjunctival malignancies with acceptable local tumor control.

The clinical course of OSSN and conjunctival melanoma may be complicated and unpredictable. A number of these invasive lesions are initially misdiagnosed as benign lesions such as pterygium, pinguecula, papilloma and amelanotic or melanotic nevus of conjunctiva. In some cases, it may even be difficult to histologically differentiate them among the benign tumors.^{2,3}

Although the basis of conjunctival epithelial tumor treatment is total tumor excision with a safe surgical margin, different studies suggest that additive adjuvant therapy will decrease the rate of recurrence.^{2,3}

The most common supplement treatments are cryotherapy, radiotherapy and chemotherapy with different topical agents.^{5,6,19}

During the last decades, plaque radiotherapy has been used as an adjuvant modality in treatment of conjunctival epithelial malignancies. Different isotopes including strontium-90, RU-106 and iodine-125 with a target dose of 30 Gy to more than 100 Gy have been recommended. However, the suggested dose of 100 Gy by Char and his colleagues³ is comparable with mean dose of 95 Gy in our study. Because of high incidence rate of recurrent lesion following brachytherapy alone (up to 47%),⁴ most studies are suggestive of using the plaque radiotherapy as an adjunctive therapy after surgical resection of tumor.

Local recurrence of SCC has been reported in 2.3% of patients after excisional biopsy and adjuvant brachytherapy with

strontium-90 plaques.¹³ Observation of no recurrent tumor in our study may be explained by small sample size with short follow-up time. Radiation complications, particularly incidence of cataract and scleral damages, have been reported in less than five percent of cases. The presence of dry eye in one of our cases may be due to multiple conjunctival excisional biopsies or radiation complications.

Conclusion

Preliminary result of our study showed that adjunctive plaque radiotherapy in selected conjunctival SCC and melanoma appears to be a reasonable alternative method with acceptable local control and tolerable morbidity. The average follow-up time in our study was only 32 months. An extended follow-up time is needed to certainly deduce the possibility of recurrent lesions.

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