



ELECTRON THERAPY IN KELOID MANAGEMENT: A SINGLE INSTITUTIONAL RETROSPECTIVE STUDY

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ABSTRACT

Background: Keloids are benign dermal tumours composed of disorganised thick hyalinised collagen which causes aesthetic disfigurement and can be pruritic or tender. The common areas prone to develop keloids are the earlobe, upper back and midline of the chest. The treatment of keloid is complex as simple excision alone results in 45% to 100% recurrence rate. Many adjuvant therapies including

radiation has been tried to reduce the rate of recurrence. Postoperative irradiation to a minimal dose of 10-15 Gy can reduce this recurrence rate to 2.4 to 20 % with good cosmetic results. **Aims:** To study the efficacy and toxicity of adjuvant external beam radiotherapy in our patients with recurrent keloids. **Methods and Material:** A retrospective review of 15 patients with recurrent keloids, who underwent postoperative electron beam irradiation between February 1, 2011 and December 31st, 2015 was done. All the patients were treated with 4 to 6 MeV electron beam radiation using a dose schedule of 16Gy/4# within 72 hours of surgical excision. They were further analysed for control rate and toxicity. **Results:** Majority of the patients were female and anterior chest wall was the most common site of keloid formation. Intralesional steroid, 5FU or Bleomycin was used in 12 (80%) of the patients as adjuvant treatment after surgery. All the patients received radiation within three days of excision. The radiation was well tolerated in all the patients. Burning sensation, redness, pain and hypopigmentation was the side effects seen. Recurrence was seen in one patient after 6 months of Radiation. **Limitations:** Few number of patients and short follow-up period. **Conclusions:** The results of the present study indicate that hypofractionated electron

radiotherapy has an effective role as an adjuvant therapy following surgical excision of keloids in recurrent cases.

KEYWORDS: Keloids, Surgery, Recurrence, Radiation, Electrons.

INTRODUCTION

The term *keloid*, meaning "crab claw," was first coined by Alibert in 1806, in an attempt to illustrate the way in which the lesions expand laterally from the original scar into normal tissue.^[1] Keloids are benign dermal fibroproliferative tumours with no malignant potential which occurs as an abnormal response to injury. The first description of such abnormal scar formation in the form of keloids was recorded in the Smith papyrus regarding surgical techniques in Egypt around 1700 BC.^[2] The defining characteristics are the growth of the scar outside the area of injury. The scar is composed of disorganised thick hyalinised collagen.^[3] It causes not only aesthetic disfigurement but at times can be pruritic, tender and sometimes complicated by secondary infections.^[4] It can occur at any site but some areas are more prone to develop keloids. These areas are the earlobe, upper back, midline of the chest.^[5] The important risk factors for development of keloids are wound healing by secondary intention especially if the healing time is more than 3 weeks. Wounds subjected to prolonged inflammation whether due to foreign body, repeated trauma, infection, burn or inadequate wound closure are at risk of abnormal scar formation. Besides, spontaneous keloids can also occur because of genetic and race specific predisposition in some individuals.^[6,7] The treatment of keloids is complex as simple excision alone results in 45% to 100% recurrence rate.^[8] Ways to help minimize the rate of recurrence following surgical removal of keloids include cryosurgery, laser destruction, hyaluronidase, Nitrogen mustard, methotrexate, steroid injection, 5 FU, Bleomycin, retinoic acid, zinc, antihistamines, compression splints and dermabrasion.^[9] However, none of these adjuvant therapies have been proven to be 100% efficacious and the recurrence rate is more than 50%. Radiotherapy as an adjuvant therapy was introduced in 1906¹ and since then it has been proven to be one of the most effective treatment therapy for preventing recurrence.^[10-12]

The common social practice of ear piercing among females in our society often results in the formation of keloids over ear lobes. Besides, common problems like abscess and cuts are usually managed by local quacks. Because of improper incision, sutures and inadequate antibiotic coverage there is delayed wound healing which at times result in hypertrophic scar and keloids. These patients often seek treatment for cosmesis or symptomatic relief of

itching, swelling and pain. Availability of few radiation machines and the theoretical risk of carcinogenesis is the major limiting factor for the use of radiation as an adjuvant treatment modality for recurrent keloids in our part of the country. So, this retrospective analysis was conducted to assess the effectiveness and safety of radiation in these patients, before radiation could be routinely incorporated in our patients. Thus the present work is designed to study the efficacy and toxicity of adjuvant radiotherapy in patients with recurrent keloids at a tertiary cancer hospital.

METHODS AND MATERIAL

The present study is a retrospective analysis of all the patients with recurrent keloids treated with radiation in the department of Radiotherapy of Mahavir Cancer Sansthan, Patna from 1st February 2011 to 31st December 2015. A total of 15 patients received adjuvant radiotherapy during the given study period. A signed consent form was obtained from each patient before starting the treatment. All the patients were post-operative cases and received planned adjuvant radiation within 24 to 72 hours of surgery. The target volume included the scar with 0.5 to 1cm margin all around. Non target areas were shielded using customised lead cut out. Radiation was delivered using 4 to 6 MeV electron beam at an SSD of 100cm on Elekta Synergy linear accelerator. Bolus was used as required. The dose fraction schedule used was 16Gy/4# @ 4Gy per fraction. All the patients were kept on regular follow up to evaluate local control and late sequelae.

RESULTS

All the patients were from the state of Bihar. The age of the patients ranged from 18 to 65 years. The median age was 48 years. 66.67% of the patients were female and 33.33% were male. The most common site involved was anterior chest wall (46.66%). The second most common site was the ear lobe (26.6%). The other sites were preauricular area, angle of mandible, lt. knee and bilateral gluteal region in one patient each.

Eighty percent of the patients were operated twice, and remaining twenty percent thrice for recurrence of the keloid before being treated with adjuvant radiation at our centre. Twelve of these patients were also given Intralesional steroids after surgery. Along with steroids, two of the patients had also received 5FU. Another two patients received Bleomycin with steroid as an adjuvant treatment to prevent recurrence.

Four patients received radiation within 24 hours, eight within 48 hours and remaining three within 72 hours of surgical excision. All patients received radiation to a total dose of 16Gy in 4 fractions @ 4Gy per fraction per day with 4 or 6 MeV electrons. The patients were treated continuously for 4 days without any treatment gap. Radiation was well tolerated in all the patients.

One of the patient complained of mild burning sensation over the scar from the third day of treatment which subsided after two weeks. Three patients complained of mild redness and pain at the scar site during radiation which subsided spontaneously about 1 week after completion of radiation. Hypopigmentation was observed in 2 patients at the scar site after 4 and 6 months respectively. No other significant late sequelae were noted. One of the patient had a local recurrence 6 months after radiation, which was treated with reexcision.

The characteristics of the patients and their treatment are summarised in Table 1.

Table 1.

S.No	Age yrs.	Sex	Site	Previous Surgeries (Number)	Any other treatment	RT Dose	Status at LFU
1	18	F	Lt. Pre auricular area	2	No	16Gy/4#	LRC
2	24	F	Ant. Chest wall	2	5-FU & Steroid	16Gy/4#	LRC
3	28	M	Angle of Mandible	2	Steroid	16Gy/4#	LRC
4	36	M	Ant. Chest wall	3	Steroid	16Gy/4#	local recurrence
5	40	M	Ant. Chest wall	2	No	16Gy/4#	LRC
6	54	F	Ear lobe	2	Bleomycin & Steroid	16Gy/4#	LRC
7	60	M	Lt. Knee	2	Steroid	16Gy/4#	LRC
8	65	F	Ant. Chest wall	2	No	16Gy/4#	LRC
9	48	F	Ant. Chest wall	3	Steroid	16Gy/4#	LRC
10	56	F	Ant. Chest wall	2	Bleomycin & Steroid	16Gy/4#	LRC
11	63	M	B/L Gluteal region	2	Steroid	16Gy/4#	LRC
12	65	F	Ear lobe	3	5-FU & Steroid	16Gy/4#	LRC
13	48	F	Ant. Chest wall	2	Steroid	16Gy/4#	LRC
14	50	F	Ear lobe	2	Steroid	16Gy/4#	LRC
15	38	F	Ear lobe	2	Steroid	16Gy/4#	LRC

DISCUSSION

Keloids are dermal fibrotic lesions that are a variation of the normal process of wound healing. The excessive proliferation of normal tissue healing process results from the loss of

normal control mechanism that regulates the balance between tissue repair and regeneration. The production of extracellular matrix proteins, collagen, elastin, and proteoglycan presumably is due to prolonged inflammatory process in the wound.^[13] The occurrence of keloids and hypertrophic scars has equal sex distribution.^[14] However, in our study there were 66.67% female patients. The probable cause could be the cosmetic implications associated with the disfigurement caused by recurrent keloids.

The most common site seen in our study was anterior chest wall, which accounted for 46.66% of the patients. This is in accordance to the fact that keloids are common in areas subjected to high skin tension like the skin over sternum. However a study by Song et al showed ear lobes as the most frequent site of keloids. The difference could be because 83.33% of their patients were female and ear piercing is a common custom highly prevalent among the female population of Asia.^[15] In our study, ear lobe was the second most common site.

Local excision is the primary treatment most commonly used to treat keloids. However, with surgical resection only, keloids have up to 90% recurrence and so adjuvant treatment has been recommended.^[16,17] Intralesional injection of corticosteroids is one of the mainstays of keloid treatment. Corticosteroids are believed to act by decreasing the level of collagenase inhibitors, thereby increasing collagen degradation with the preferred drug being triamcinoloneacetonide at a dose of 20–40 mg/ml.^[18] Although success rates increased with combination of surgery and steroids, the results show great variation cross different studies and most of them are not satisfactory.^[19] The search for another effective therapy lead to the use of radiation in these cases. The effects of radiation on keloids are thought to be mediated through inhibition of neovascular buds and proliferating fibroblasts, which result in decreased collagen production.^[20] Postoperative irradiation to a minimal dose of 10-15 Gy can reduce this recurrence rate to 2.4 to 20 % and good cosmetic results are obtained in 15to 18%^[11,21] Many trials have shown the efficacy of radiation in various dose and schedules in treating recurrent keloids. Kovalic et al^[12] reported control rates between 73 to 93% in 113 keloids treated with post operative radiation. Another similiar study by Borok et al^[11] reported the control rate to be 97.6% in 393 cases. Scalfani et al^[22] reported a recurrence rate of 33% when surgery was combined with corticosteroids, which decreased to only 12.5% when adjuvant radiation was used instead. Currently, as per International clinical recommendation for scar management radiation is considered to be the most effective treatment available for

recurrent keloids.^[23] Radiation can be delivered by brachytherapy or external beam radiotherapy. Brachytherapy can be delivered by LDR^[24] or HDR^[25] technique using Iridium¹⁹² or Strontium⁹⁰.²⁶ External beam radiation can be given by low energy x-rays or electrons. All the patients in our study were treated with 4 to 6MeV electrons. As per review published in 2011 by Gupta et al electron beam therapy is considered the most successful radiation modality for treating keloid.^[26] Radiotherapy is now recommended in cases of repeat recurrences postoperatively or where there is a high-risk of recurrence (e.g., marginal resection, large lesion, unfavourable location)

Most of our patients received radiation within 48 hours of surgery, though the duration ranged from 24 to 72 hours. Studies have shown that the most effective time for administering radiation is immediately after or within 24 to 48 hours of surgical removal of the keloid.^[20,26] There is no benefit of giving radiation before surgery as the keloid is made up of biologically inert collagen, a hypoxic environment, and hypoxic fibroblasts. Post-operative radiotherapy for keloids is largely successful because the post-operative target is the well oxygenated, neo-vascularized, replicating fibroblasts, which are relatively more sensitive to fractionated radiotherapy than quiescent hypoxic resting fibroblasts of keloidal tissues. Larger fraction- sized radiation produces better results than standard 200 cGy daily fractionation.^[27,28] All our patients received 16Gy in 4 fractions @ 4Gy per fraction. The optimal dose schedule is still unclear with no uniform consensus on total dose and fractionation required for the treatment of recurrent keloids. However, the recommended total dose is 12 to 20 Gy in divided fractions. The commonly used protocols are: 5Gy in 3 fractions or 4Gy in 4 fractions daily. Single dose radiotherapy with 7.5Gy to 10Gy is also effective but is not used commonly because of the theoretical risk of secondary carcinogenesis.

Radiation was well tolerated in all the patients. One of the patient complained of mild burning sensation over the scar which subsided after two weeks. Three patients complained of mild redness and pain at the scar site. This is in accordance with the side effects reported in literature which includes redness, rash, tingling, burning sensation, hyperpigmentation and hypopigmentation of the skin.^[26] Hypopigmentation was observed in 2 patients at the scar site. No other significant late sequelae were seen. One of the patient developed local recurrence 6 months after radiation, which was salvaged by surgery.

Historically, Radiation has been known to be a carcinogen and increases the risk of developing cancer. Despite the potential risk of carcinogenesis with the use of radiation, a number of large studies have not reported any case of radiation induced cancer in patients with recurrent keloids. A study by Ogawa et al for the risk of carcinogenesis associated with the use of radiation for recurrent keloids concluded that the small volume irradiated during the treatment of keloids makes the risk of radiation induced tumour almost negligible. However adequate planning is to be done to provide adequate protection of surrounding tissues like thyroid and breast, especially in children.^[29] The use of electrons in delivering radiation, with a rapid dose fall off provides further protection to the normal tissues that has further decreased the chances of carcinogenesis. Radiotherapy following surgical excision is one of the most effective and acceptable treatment modality available in the management of recurrent keloids and remains the treatment of choice for most patients.^[30]

CONCLUSION

Post-operative electron radiotherapy seems to be well tolerated and effective treatment for recurrent keloids. However longer follow up and more number of patients is required to establish the safety and efficacy of adjuvant electron therapy in the prevention of recurrent keloids.

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