Treatment of Keloids with Surgery and Immediate Postoperative Radiotherapy: Knowledge Gained Over 17 Years

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Abstract

Background The treatment of keloidal scars with radiotherapy has been practiced for more than a century. Radiotherapy post-surgery has been deemed necessary and effective in preventing recurrence but still, no clear guidelines exist as to the best modality of radiotherapy, the ideal dose, and the time it should be given for keloidal scars. The purpose of this study is to confirm the effectiveness of this treatment and address these issues.

Methods Since 2004, 120 patients presenting with keloidal scars were seen by the author. Out of them, 50 were managed with surgery followed by HDR brachytherapy/electron beam radiotherapy delivering 2000 rads to the scar within 24 hours of surgery. Patients were followed up for at least 18 months to assess the scar status and the recurrence of keloids. Recurrence was defined as the appearance of a nodule or an obvious return of the keloid within 1 year of treatment.

Results Three patients developed a nodule in the scar, which was deemed a recurrence, making an incidence of 6%. There was no major problem after immediate postoperative radiotherapy. Five patients had delayed healing at 2 weeks and a hypertrophic scar was noted in five patients at 4 weeks that settled with conservative measures.

Conclusion Treating the vexing problem of keloids with surgery and immediate postoperative radiotherapy is safe and effective. We recommend that this be adopted as the standard treatment in keloid management.

Keywords
- keloid
- brachytherapy
- radiotherapy
- hypertrophic scar
- keloid excision

Introduction

The treatment of keloids is a vexing experience due to its high propensity to recur even after complete surgical excision, the recurrence rate being as high as 45% to 100% [1,2]

Surgery followed by radiotherapy (RT) has been widely reported as the most effective modality of treatment with control rates at 1 year of about 85 to 90%.[3] However, the traditional problems with any radiation therapy have been the irradiation of surrounding normal areas and the remote chance of developing secondary cancer.[2]

High dose-rate (HDR) brachytherapy that allows pinpoint deposition of radiation to tissues, at the desired site and depth only, provides an answer to the above problems.[4]

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Many studies have quoted particularly good control rates with no major side effects. But then, the ideal time frame to give the radiation, the minimum effective dose, and the other methods of radiation apart from HDR brachytherapy that may be equally effective, have not been clearly defined as of now. This study aims to address these issues

While much literature is available, we could not find reports of a long-term follow-up after surgery and immediate postoperative radiotherapy from India.

Patients and Methods

From 2004 to 2021, 120 patients who came for a consultation with keloidal scars to the out-patient department of a tertiary government hospital and a referral private multi-specialty hospital were evaluated. The history (duration, site, inciting event, symptoms, previous treatment history, family history) and the clinical features (site, size, maturity, quality of surrounding skin, similar lesions elsewhere, ulcers, infection) were noted. In 24 patients (3 with ear keloids and 21 with recurrent keloids post-surgery done elsewhere) excision with immediate postoperative radiotherapy was offered as the primary treatment. In all others, silicone gels/betamethasone ointment (0.1% w/w) massage twice daily with pressure therapy was the first line of treatment given. The various treatments used subsequently such as silicone gel sheets and intralesional steroid injections are enumerated in ►**Fig. 1**. In total, 26 patients who did not respond to the conservative methods were offered surgery and enrolled in the study making a total of 50 patients who underwent surgery plus postoperative radiotherapy. An informed consent explaining the treatment plan, side effects/risks, and the necessity of strict follow-up, was obtained from all patients.

The keloid was excised extralesionally in 45 patients. In five cases, with large, multiple keloids, intralesional excision was done (►**Fig. 2**). Primary closure was done in 48 cases using absorbable polyglactin or polydioxanone for subdermal sutures in 25 patients, nonabsorbable subcuticular in 9 patients, or simple sutures. Two patients with pre-sternal keloids required split skin grafting for wound cover.

All patients received HDR brachytherapy/electron beam radiotherapy to the suture line starting within 24 hours of surgery. In 10 patients, HDR brachytherapy was given by

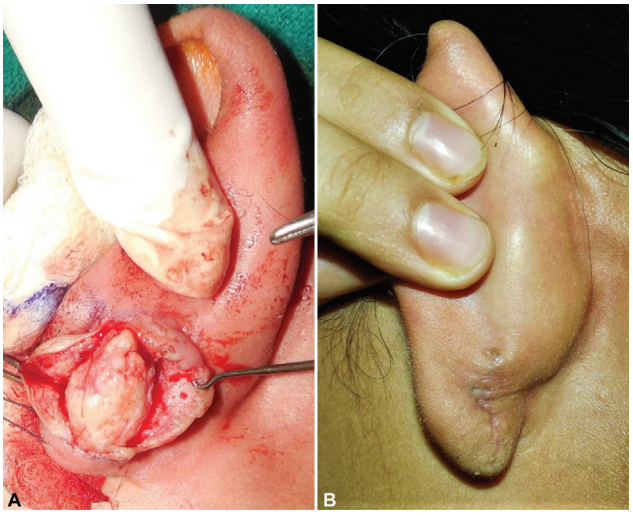

Fig. 2 : Intra-keloidal excision of large earlobe keloid (**A**) and 6 months postoperative image (**B**).

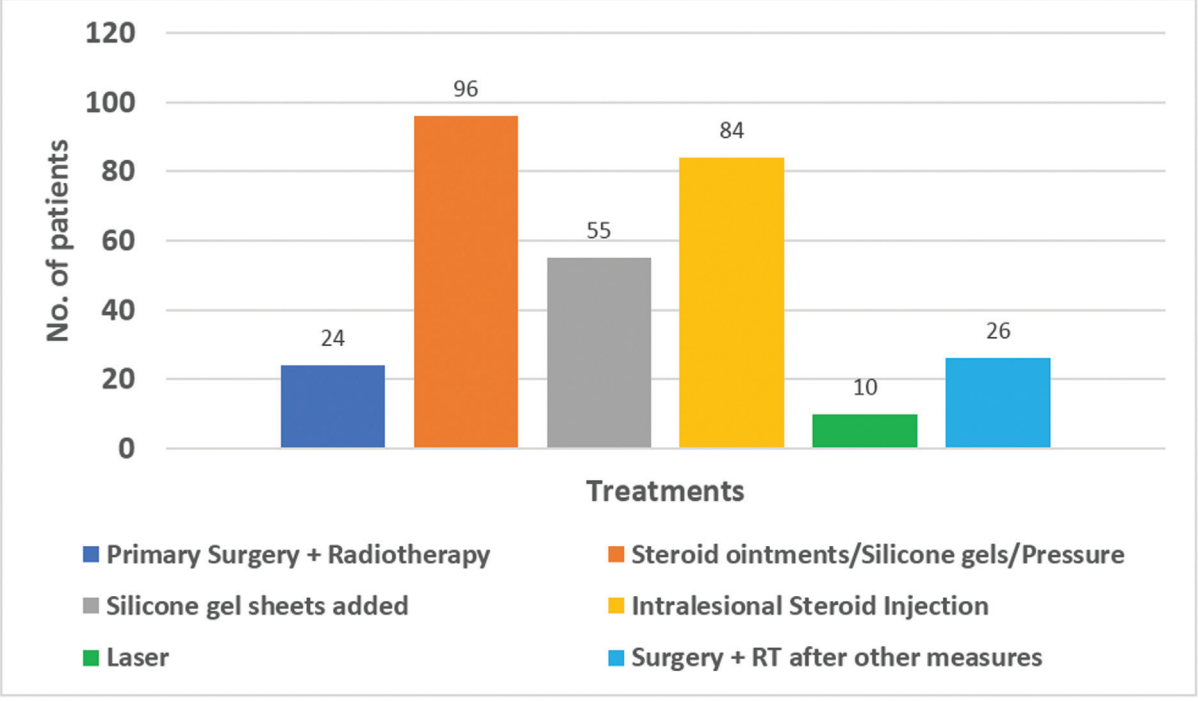

Fig. 1 Treatment offered to 120 patients.

Fig. 3 Dental compound Mould with micro-catheters (**A**), microcatheters placed on either side of scar (**B**), micro catheters attached to HDR Brachytherapy unit (**C**), electron therapy with linear accelerator in contact with scar (**D**). HDR, High dose-rate.

making a 2-layer mold of the operated site using dental compound, two microcatheters were sandwiched within it and fixed at 1 cm distance from each other. The mold was firmly strapped to the operated site, such that the catheters were placed at a distance of 5 mm on either side of the suture line. These catheters were then attached to the HDR brachytherapy unit that was kept close to the target, i.e., the suture line. Iridium 192 seeds were passed through it using a remote after-loading technique (►**Fig. 3**). A total dose of 20 Gy in four fractions of 5 Gy was administered, starting on the zero postoperative day, with a minimum of 6 hours gap between fractions and the treatment was completed within 72 hours of surgery. Each fraction was delivered in 5 to 8 minutes.

In 40 patients, electron beam radiotherapy was given with a linear accelerator delivering 2000 rads in fractions to the dermis at the suture line using a 6 MeV machine. The source was kept in close contact with the operated area, the beam was centered and collimated on the suture line and all surrounding tissues were shielded with lead bars (►**Fig. 3D**). The treatment was initiated within 24 hours of surgery and the number of fractions was decided by the radiotherapist.

In all cases, the applied radiation dose was 100% at the Dmax, which was at the skin surface in this superficial therapy. The 90% isodose target area was the operated scar. In HDR brachytherapy, the maximum depth of penetration of radiation was 0.5 cm, and 0.5 to1 cm in a linear accelerator. In cases where both the front and the back sides had to be irradiated, for example in the earlobes, the depth of penetration was fixed at 2 cm.

Sutures were removed when the wound healed well, usually between the 7th to the 10th postoperative day. All patients were routinely prescribed compression garments/pressure earrings.

Patients were followed up weekly for the first 2 weeks, once a month for the first 3 months, then every 3 months for 1 year, and then every 6 months as required. During each visit, any scar widening or hypertrophy, wound-related complaints, skin condition, and recurrence of keloid at the surgery site were noted.

Results

Of the 50 patients, 40 were women and 10 were men mostly aged between 21 and 30 years. The duration of the keloids ranged from 6 months to a maximum of 18 years (►**Table 1**).

Table 1 Profile of patients who underwent surgery with RT

No.	Age	Sex	Site	Duration	Previous treatments		
					Surgery	Steroid Injections	Others
1	26	F	Ear	7 months	Once	No	Nil
2	15	M	Shoulder	4 y	Once	7	Silicone gel/steroid ointment/pressure
3	40	F	Ear	3 y	No	No	No
4	40	F	Ear	2 y	Once	No	No
5	35	F	Ear	6 months	No	No	No
6	17	F	Ear	2 y	No	No	No
7	28	F	Ear	18 y	2	2	No
8	18	F	Ear	15 y	2	2	Homeopathy/Acupuncture
9	30	F	Face	12 y	3	3	Silicone gel/ Steroid Ointment/Silicone gel sheet
10	17	M	Neck	12 y	2	2	No
11	21	F	Chest	2 y	Once	Once	Nil
12	30	F	Ear	3 y	Once	No	No
13	45	F	Ear	3 y	Once	No	No
14	18	F	Ear	1 y	Once	Once	No
15	32	F	Ear	2 y	Once	Nil	Local remedies
16	23	M	Chest	5 y	No	2	Silicone gel/ Steroid Ointment/Pressure
17	20	F	Neck	4 y	Once	3	No
18	30	F	Ear	1 y	No	2	Silicone gel/ Steroid Ointment
19	26	F	Ear	2 y	No	1	Silicone gel/ Steroid Ointment
20	17	M	Neck	3 y	No	3	Silicone gel/ Steroid Ointment
21	20	F	Leg	5 y	No	2	Silicone gel/ Steroid Ointment
22	18	F	Shoulder	3 y	No	5	Silicone gel/ Steroid Ointment/Silicone Gel Sheet
23	23	F	Ear	2 y	No	2	Silicone gel/ Steroid Ointment
24	24	F	Ear	3 y	No	1	Silicone gel/ Steroid Ointment
25	25	F	Ears, Cheek	2 y	No	2	Silicone gel/ Steroid Ointment/Pressure
26	23	F	Ear	4 y	No	7	Ointments
27	18	F	Ear	7 y	No	3	Antibiotic-Steroid Ointment
28	26	F	Cheek	3 y	No	2	Silicone gel/ Steroid Ointment/Pressure
29	28	F	Back	2 y	No	3	Silicone gel/ Steroid Ointment/Silicone Gel Sheet
30	16	F	Ear	6 y	No	4	Silicone gel/ Steroid Ointment
31	18	F	Ear	5 y	No	No	Silicone gel/ Steroid Ointments
32	28	F	Cheek	3 y	No	1	Silicone gel/ Steroid Ointment/Silicone Gel Sheet
33	22	F	Ear	2 y	No	3	Silicone gel/ Steroid Ointment
34	25	F	Ear	4 y	No	1	Silicone gel/ Steroid Ointment
35	38	F	Chest	4 y	No	3	Silicone gel/ Steroid Ointment/Silicone Gel sheet
36	40	F	Cheek	4 y	No	2	Silicone gel/ Steroid Ointments/Pressure
37	9	F	Ear	6 y	No	4	Silicone gel/ Steroid Ointments
38	24	F	Ear	4 y	Once	No	No
39	35	F	Chest	10 y	No	5	Silicone gel/ Steroid Ointment/Silicone Gel sheet
40	32	M	Chest	10 y	No	4	Silicone gel/ Steroid Ointment/Pressure
41	38	F	Breast	3 y	Once	3	No
42	27	M	Abdomen	5 y	Once	2	No

Table 1 (*Continued*)

No.	Age	Sex	Site	Duration	Previous treatments		
43	12	M	Cheek	3 y	Once	No	No
44	20	M	Shoulder	7 y	Once	No	No
45	15	F	Foot	2 y	No	No	Silicone gel/ Steroid Ointment/Pressure
46	42	M	Chin	2 y	No	3	Silicone gel/ Steroid Ointment/Silicone Gel sheet
47	36	F	Hand	5 y	Once	2	No
48	28	F	Abdomen	3 y	No	3	Silicone gel/ Steroid Ointment/Pressure
49	25	M	Forearm	10 y	Once	4	Silicone gel/ Steroid Ointment/Pressure
50	22	F	Neck	10 y	Once	No	Silicone gel/ Steroid Ointment/Silicone Gel Sheet

The ear was most commonly involved; in 24 out of 50 cases (►**Fig. 4**), the exact sites being the helix/antihelix (site of secondary ear-boring) in 12 cases, the ear lobule in 11, and both areas had keloids in one. In seven cases, both the anterior and posterior surfaces of the ear were affected.

Fig. 4 Multiple helical keloids (**A**) and 1-year post-op pic (**B**). Thrice recurrent ear lobule keloid (**C**) and 1 year after excision and radiotherapy (**D**)

Seven patients had bilateral involvement. Of these, both sides were operated upon in four(2 with helical keloids and 2 with lobular keloids) but only one side was irradiated, the other side, therefore, acting as a control. The other three patients had bilateral, multiple large keloids destroying the ears and so only one side was operated upon. The other sites of keloid scars were the face in 7, chest in 5, neck in 4, shoulder in 3, upper limb, lower limb, and abdomen in 2 each, and the back and breast 1 each (►**Table 1**).

Trauma and infection were found to be the most common inciting events. Trauma ranged from minor injury (a nail scratch) to significant trauma such as a cut with a metal sheet. The initiating causes were ear-boring in 18, infection (complicating ear boring, boils, chicken pox, acne) in 10, trauma (excluding surgery) in 17, post allergic dermatitis in 2 (one in the ear lobule and another around the breast), and surgery (ear lobe repair, fracture fixation, ankle laceration repair) in 3.

All patients solicited treatment because of the unsightly nature of the keloid and the steady increase in size. The most common complaints are illustrated in ►**Fig. 5**.

There was a wide range in the sizes of the lesions, varying from a 5 mm × 5 mm ear lobule keloid to a 13 cm × 1 cm keloid on the abdomen. Immature keloids that were erythematous and blanched on pressure were found in 10, whereas the rest were firm to hard mature lesions.

Twenty-one out of 50 cases presented with excision of the keloid done elsewhere and had since recurred. Three of them had been operated on twice and one case thrice before. Similarly, 36 of the 50 patients had intralesional steroid injections, and 29 had been injected many times over multiple courses (►**Table 1**). No patient had been treated with radiotherapy before.

There were no major problems in any patient during the administration of radiotherapy but for some tenderness due to the handling of the operated scar. The clinical image during the follow-up period is depicted in ►**Table 2**.

In all cases, histopathology showed haphazardly arranged thickened hyalinized collagen, with nodules and fibrous fascicles in the reticular dermis with a normal appearing epidermis and papillary dermis suggestive of keloid.

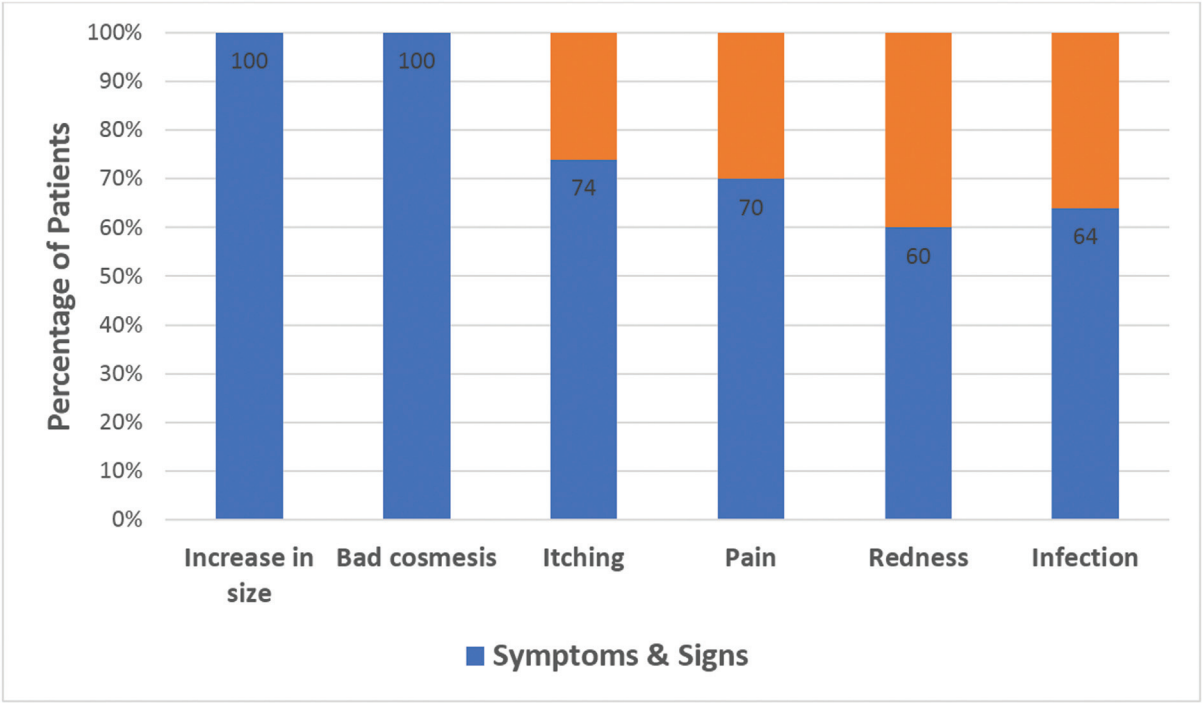

Fig. 5 Symptoms and signs in the 50 study patients.

Table 2 Signs and symptoms at follow-up after surgery and radiotherapy

Time	Pain	Itching	Delayed wound healing / scar widening	Hypertrophy	Pigment changes/ Hyperemia	Nodule/recurrence
2 weeks	No	No	5	No	4	No
4 weeks	No	1	2	5	3	No
6 months	1	2	1	1	1	1
1 year	No	2	4	1	1	2

Follow-up

Recurrence was Defined as the Appearance of a Nodule or an Obvious Return of the Keloid within one Year of Treatment

At 2 weeks, 5 patients had delayed wound healing necessitating postponement of suture removal. Four people had hyperemia and one person with a facial keloid had facial edema that settled with conservative management.

At 4 weeks, there was mild hypertrophy of the scar in five patients and widening of the scar in two patients. They were managed with scar massage and pressure therapy, and they settled to a soft pliable scar.

At 6 months, one scar on the upper chest presented as a nodule and was a hypertrophic scar at 1 year. This was deemed a recurrence. The patient was treated with a silicone gel sheet and compression garment. One patient complained of pain at 6 months, and a small stitch granuloma was observed, which subsided with the removal of remnant suture and antibiotics

At 1 year, there was a widened scar in four patients. In two patients, there was a nodule at one end of the scar, which was itchy too and therefore marked as recurrence. These patients had an anterior chest keloid and a lateral leg keloid (►**Fig. 6**). They were managed with intralesional steroids, scar massage, and pressure garments. Both settled without further aggravation of the problem within the next 6 months. In two out of four patients operated bilaterally, the non-irradiated scar developed a keloid while the side that received the RT healed uneventfully (►**Fig. 7**).

In this series, only three cases were registered as treatment failure giving a recurrence rate of 6%. The control of ear lobe keloids was **100%** at 1 year. The complications encountered during therapy were all minor and transient. The histopathology report did not help in predicting recurrence. The recurrences were also not catastrophic and could be managed with simple conservative measures to obtain a stable scar.

Discussion

Keloids are a challenge to treat and any single modality treatment like surgery alone or intralesional steroids alone

Fig. 6 Recurrence in an anterior chest and a lateral leg keloid at one year. (**A**) Preoperative chest keloid. (**B**) At 1-month postoperatively. (**C**) Recurrence as a nodular hypertrophic scar at 1 year. (**D**) Preoperative leg keloid. (**E**) 3 months postoperative. (**F**) Wide nodular recurrence at 1-year postoperatively

is fraught with high (80%) unacceptable recurrent lesions.[5–7] And so, combination therapy is preferred.[8]

Several therapies including lasers, interferons, calcineurin inhibitors, verapamil, bleomycin, 5-flurouracil creams, retinoic acid, tacrolimus, botulinum toxin, imiquimod, fat grafting, stem cell therapy, RNA-based therapies and agents that affect collagen synthesis are being used with varying success.[1,6]

However, the treatment that is accessible and has consistently given the best results in controlling recurrence, leaving an acceptable scar is surgery followed by radiotherapy.[9,10]

Core excisions or wedge excisions, otherwise called intralesional excisions can be done to reduce distortion and tension in the wound and to give an acceptable cosmetic result.[2,11] The rationale being surgery will be combined with another modality such as radiotherapy for local control. In five cases, with multiple large keloids, intralesional excisions were done to preserve available normal skin and none developed a recurrence. Though aggressive use of cautery for excision and crushing of the tissues is to be avoided, the most important principle in surgery to minimize the chance of recurrence is reducing wound tension. This should be achieved by suturing the fascia, subcutaneous and dermal layers, incorporating Z-plasty, skin grafting, or local flaps as required.[11–13] In this series, though one patient developed a stitch granuloma on a retained suture, the wound healed well without any ill effects.

Radiotherapy acts on keloids by inducing apoptosis, preventing an accelerated repopulation of fibroblasts, and suppressing angiogenesis in the wound.[14,15] Excessive expression of lymphocytes and macrophages is also prevented thereby stopping chronic inflammation.[15]

Ollestein et al were the first to show that immediate postoperative radiation therapy reduces recurrence rates.[16]

HDR brachytherapy by virtue of being able to deliver the required dose precisely to the scar site is highly effective.[4,17,18] As HDR brachytherapy units are available only in specialized centers, there has been a trend to use electron or photon beams from a linear accelerator. Electron beams are used preferentially for treating keloids as the maximum dose deposition occurs near the surface. The dose then decreases rapidly with depth, sparing underlying tissue.[19]

Many studies have found no difference in the ease of use, the side effects such as hyperemia or pigment changes, or the rates of recurrence between HDR brachytherapy and External beam therapy.[20–22] We have used both modalities as were available and suitable for each case. All the children in this study were given electron beam radiotherapy and they tolerated it well without panicking or fidgeting, maybe because it is painless.

The dose and the timing of radiotherapy are very important in getting optimum results. Radiotherapy should be started within the first 24 hours of surgery [17,23] to be maximally effective. The biological effective dose (BED) at the scar site is also an important factor in preventing recurrence. When a single 8 Gy dose was given, there was a recurrence of 16.2%.[24] The optimal treatment is perhaps a BED dose of 30 Gy, which gives a recurrence of less than 10%. This can be achieved by a single acute dose of 13 Gy, two fractions of 8 Gy or three fractions of 6 Gy, or a single dose of 27 Gy at a low dose rate.[25] While higher doses result in higher

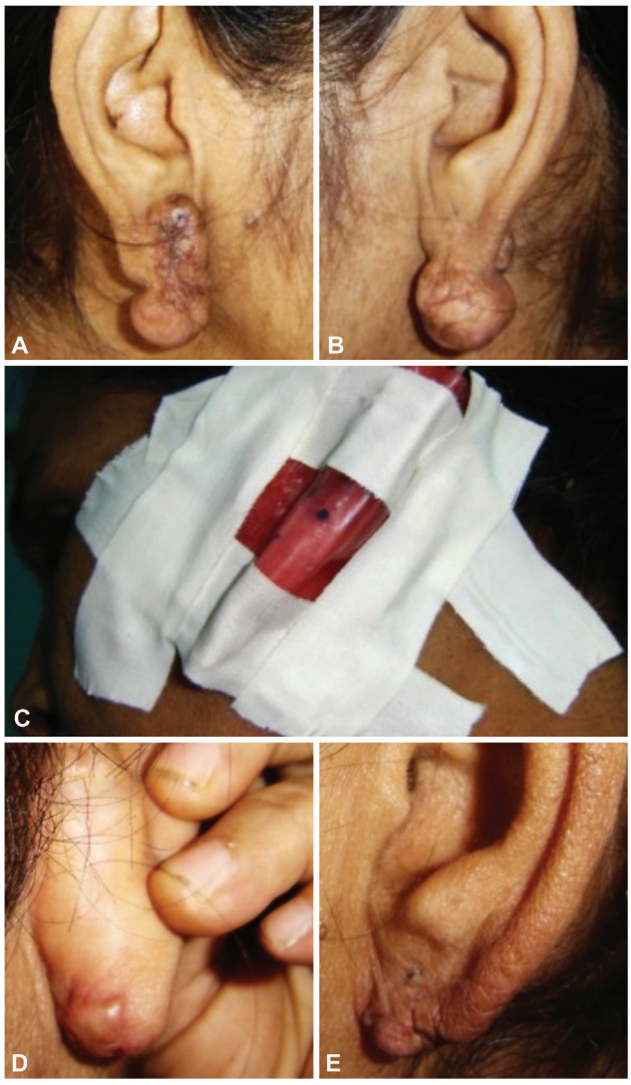

Fig. 7 Bilateral ear lobule keloids. (**A**): R side preoperative. (**B**) Left side preoperative. (**C**) Left side irradiated post-surgery. (**D**) Recurrent keloid in control R ear at 1-year postoperative. (**E**) No recurrence in the left ear at 1-year postoperative.

adverse effects such as erythema and wound dehiscence, recurrence rates increased from 11% to 43% when the dose was under 20 Gy in five fractions.[26]

A dose of 20 Gy in four or five fractions provides a safe and effective method of delivering radiotherapy[27] and that is what we followed. The three recurrences that we saw, were in areas of high stretch tension (the anterior chest and near a joint) as has been noted by many authors too [11,21] but they were managed conservatively. Reducing wound tension in these areas with z plasties, SSG, or local flaps, may have reduced the recurrence rate in this series.[28,29]

The only issue that remains is the question of carcinogenesis after radiation exposure for a benign disease. Many studies have analyzed this and a metanalysis did find that radiation is acceptable and effective in keloid treatment with extremely low secondary cancer risk.[29,30] In the last 17 years of this treatment being followed, no patient reported with malignancy after radiotherapy.

Conclusion

Keloids are preferentially managed by a multi-modality treatment to prevent recurrence. Immediate postoperative radiotherapy affords good scar control. HDR brachytherapy and electron beam therapy offer an ideal solution, as they can be done on an outpatient basis, with a relatively low cost and excellent radiation protection due to exact dose distribution to target tissues. An intra or extrakeloidal excision followed by 20 Gy of radiation given in fractions started within 24 hours of the surgery gives minimal wound problems, an acceptable scar, and a local control rate of 94% with no significant side effects. And so is an effective management of keloids.

Author's Contributions

N.B. contributed with conceptualization, data curation, formal analysis, methodology, validation, visualization, writing – original draft, writing – review & editing. K.B. contributed with formal analysis, methodology, supervision, validation, visualization, writing–review & editing. T.C.C. contributed with conceptualization, methodology, supervision, validation, and visualization.

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Conflict of Interest

None declared.

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