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Adjuvant single-fraction radiotherapy is safe and effective for intractable keloids

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The aim of this study was to assess the feasibility and efficacy of high-dose, single-fraction electron beam radiotherapy for therapy-resistant keloids. Before 2010, intractable keloids were treated at our institution with post-operative irradiation of 6–15 Gy in 3–5 fractionations. For convenience and cost effectiveness, we have changed our treatment protocol to high-dose single-fraction radiotherapy. A total of 12 patients with 16 keloid lesions were treated from January 2010 to January 2013 in our department. A 10-Gy dose of electron irradiation was given within 72 h of the surgical excision. The mean follow-up period was 20 months. Treatments were well tolerated, and there was no recurrence in any of the patients. Severe adverse effects were not observed. Surgical excision of the keloid, followed by immediate, single-fraction, high-dose radiotherapy, is both safe and effective in preventing recurrence of therapy-resistant keloids.

Keywords: keloid; radiation; electron beam; single fraction

INTRODUCTION

Keloids have been defined as a benign growth of dense fibrous tissue arising from an abnormal healing response to an injury and extending beyond the original borders of the wound. They are composed of an overabundant deposition of disorganized, thick, hyalinized collagen [1]. In addition to the aesthetic disfigurement, keloids can be pruritic and tender and can be complicated by secondary infection. Surgical excision alone results in 45–100% recurrence [2]. Some adjuvant treatments have been tested, including pressure treatment, intralesional steroid injection, silicone gel sheeting, and cryotherapy. None of these have demonstrated a real efficacy in preventing keloid formation, and recurrence rates are >50% [3]. Radiotherapy has been demonstrated as one of the most effective methods of preventing recurrence (recurrence rate ~20%) [3–7] and is considered to be the most effective treatment available for severe keloids, according to the international clinical recommendations on scar management [8]. However, no consensus has been reached on the optimal radiation dose and fractionation schedule. To our knowledge, the result of single-fraction external radiotherapy has not been published in Asia. Therefore, the goal of this study was to report our initial experience with high-dose single-fraction electron beam radiotherapy.

MATERIALS AND METHODS

Before 2010, intractable keloids were treated at our institution with post-operative irradiation of 6–15 Gy in 3–5 fractionations. For convenience and cost effectiveness, we have changed our treatment protocol to high-dose, single-fraction radiotherapy. A total of 12 patients with 16 keloid lesions were treated from January 2010 to January 2013 in our department. All patients had experienced several recurrences

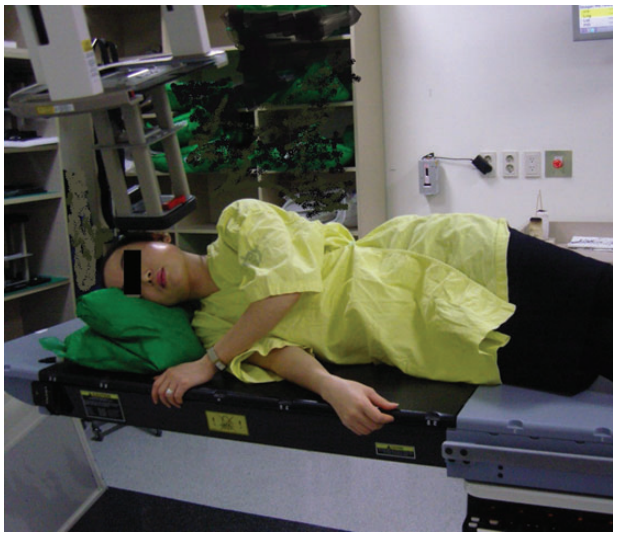

Fig. 1. Treatment setup for earlobe keloid.

after various types of treatments, including surgical excision, steroid injections, and laser therapy, but none had previously received radiotherapy. All patients were informed about the possible harmful effects of radiotherapy, including late carcinogenesis, and signed informed consent forms were obtained before the start of radiotherapy.

All keloids were extirpated completely, and the wound was closed primarily (except for in one patient) by the same plastic surgeon. A local flap was used in that patient. Adjuvant post-operative radiotherapy was given within 72 h of surgery. Irradiation with a 6-MeV electron beam administered by a linear accelerator was performed at a 100-cm source-to-skin distance. A 1-cm bolus was applied over the skin after set-up. The dose was 10 Gy applied in a single fraction. The applied dose point was 90% at the maximal dose. Radiotherapy beams were angled to be perpendicular to the skin (Fig. 1). Non-target areas were shielded with a customized lead cutout. The earlobes were taped back and shielded underneath to avoid irradiation to the skull and brain beneath. Pressure treatment and tranilast medication were given for more than 3 months, but in a few cases, medication was stopped due to side-effects such as nausea. We held telephone interviews with some patients who could not visit our hospital. The mean follow-up period was 20 months. Elevation of the lesion not confined to the original wound area was judged (by the same doctor) as recurrence.

RESULTS

The characteristics of the patients and lesions are summarized in Table 1. All patients were Asian: 10 women and 2 men, aged 20–60 years with a median age of 32 years. The location of keloid scars was the following: eight on the earlobe (50%), four on the anterior chest wall (25%), two on the shoulder (13%), one on the suprapubic region (6%), and one on the abdomen (6%). Treatments were well tolerated, and there was no recurrence in any of the patients. Severe adverse effects, such as skin peeling, wound dehiscence, and infection were not observed. Some patients experienced hyperpigmentation, but it disappeared within a year after treatment. Pre- and post-treatment photographs of keloids at various sites showed excellent cosmetic results (Figs 2–5).

Table 1. The characteristics of the patients and lesions

Median age (range)	32 (20–60)
Sex	*n* (%)
Male	2 (17)
Female	10 (83)
Location	
Earlobe	8 (50)
Anterior chest wall	4 (25)
Shoulder	2 (13)
Suprapubic	1 (6)
Abdomen	1 (6)

DISCUSSION

Treatment of intractable keloids can be complex and often requires a multimodal approach to therapy. Intralesional injection of steroid shows a 5-year response rate of only ~50% [9]. Other adjuvant treatment, including pressure treatment, silicone gel sheeting, or cryotherapy, also failed to demonstrate a real efficacy in preventing keloid formation [3]. Consistent reliable control of keloids by using radiotherapy has been reported by many authors [6, 7, 10, 11]. Although there has been no consensus with respect to the total dose and fractionation schedule in the treatment of keloids, some UK and US groups have reported on their experiences using single-fraction radiotherapy and have shown that it is a safe and convenient method of treatment with low recurrence rates [10, 12]. However, to our knowledge, the outcome for single-fraction external radiotherapy has not been published in Asia. In the present study, we showed that a single dose of 10 Gy within the first 72 h after excision of keloids is both safe and effective in all Asian patients. This treatment is simpler, more convenient, and cheaper than multiple fractionation. Electron beam radiotherapy is non-invasive and does not cause pain compared with other modalities such as intralesional steroid injection. Plastic surgeons and dermatologists may hesitate to recommend radiotherapy for keloid treatment because of the risk of radiation-induced malignancy. However, reviewing the literature, only 5 out of more than 6500 cases has been described as potential and doubtful

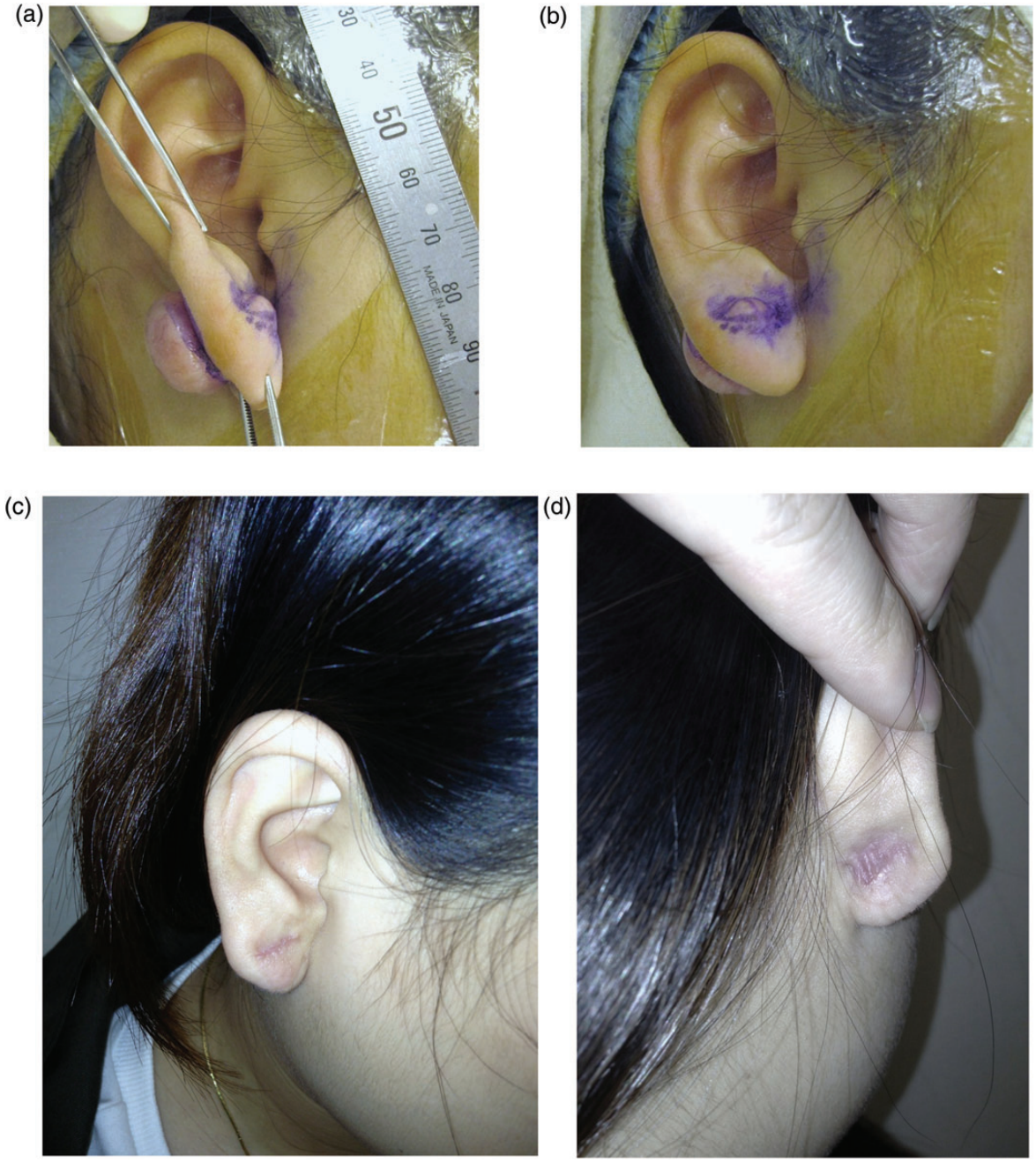

Fig. 2. A case of keloid of the earlobe (**a** and **b**) before treatment, and (**c** and **d**) 9 months after treatment.

radiation-induced malignancy [12, 13]. Despite the risk of radiation-induced malignancy being so low, we do not recommend this treatment in very young patients unless previous alternative treatments have failed for several years and the keloids cause severe pain and disfiguration.

The threshold dose and dose–response relationship for the treatment of keloids has been reported in several studies [7, 14–16]. Edsmyer *et al.* identified the threshold dose for reliable control as 12–14 Gy in a single fraction by X-ray in the post-operative setting [14]. According to Kal *et al.*, the biologically equivalent dose (BED) of the various radiotherapy regimens were calculated using the linear–quadratic concept, and the recurrence rate decreased as a function of BED in the range of BED >10 Gy. At a BED >30 Gy, the recurrence rate was <10%. Therefore, they insisted that a dose of 13 Gy, equivalent to a BED of 30 Gy, should be given for single-fraction radiotherapy. Sakamoto *et al.* also proposed 20 Gy in five fractions (BED 30 Gy) as the optimal dose for

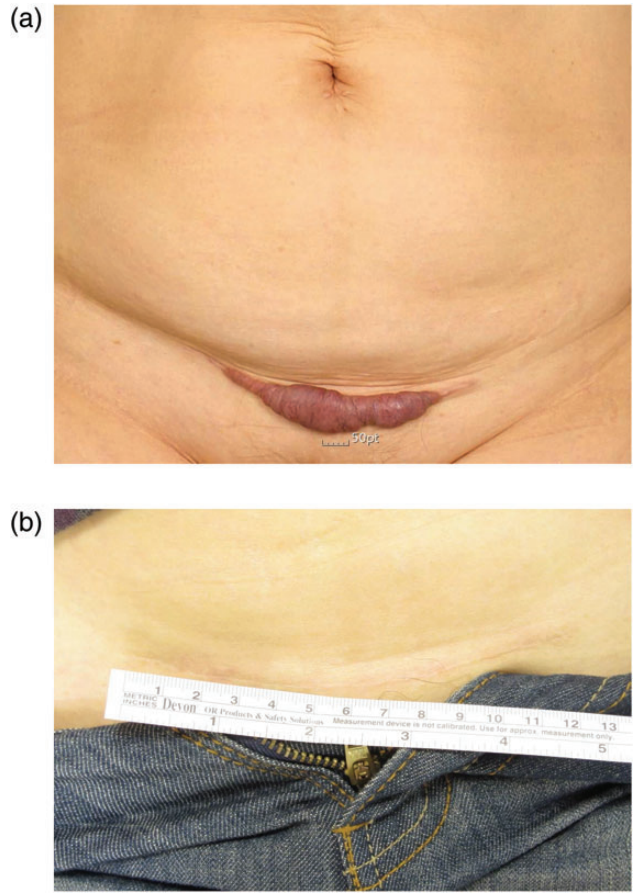

Fig. 3. A case of keloid of the suprapubic region (**a**) before treatment, and (**b**) 7 months after treatment.

the post-operative treatment of keloids [16]. In the current study, we delivered a maximal dose of 11.1 Gy (BED 23.1 Gy). That dose could be considered a suboptimal dose according to the aforementioned studies. Recently, Ogawa *et al.* published the results of an Asian study of 370 lesions of keloids and hypertrophic scars treated with surgical excision followed by electron beam radiotherapy [7]. They insisted that keloids and intractable hypertrophic scars should be treated with a range of dose schedules according to the location of lesion. They proposed 20 Gy in four fractions (BED 30 Gy) for keloids on the anterior chest wall, or in the suprapubic or scapular region, 10 Gy in two fractions (BED 15 Gy) for keloids on the earlobes, and 15 Gy in three fractions (BED 22.5 Gy) for keloids at other sites. Up till now, we have used 11.1 Gy in one fraction (BED 23.1 Gy), regardless of location. According to the study of Ogawa *et al.,* the dose we used could be too low for keloids on the anterior chest wall or in the suprapubic or scapular region, or too high for keloids on the earlobes. Because of concern about radiation-induced malignancy, and based on the evidence of other studies and the excellent outcome of the current study, we are now considering lowering the dose.

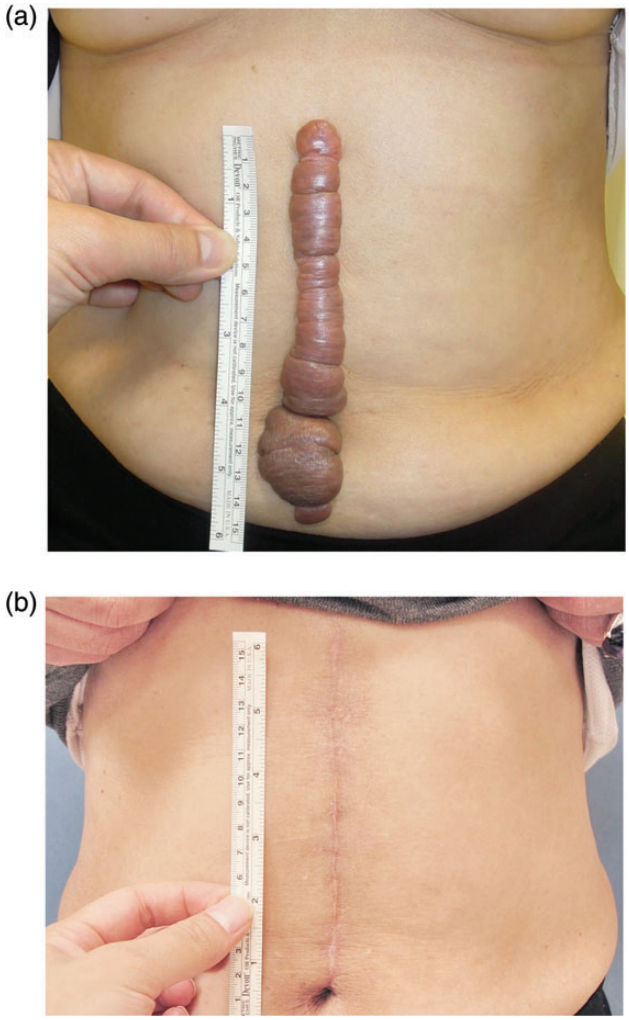

Fig. 4. A case of keloid of the abdomen (**a**) before treatment, and (**b**) 7 months after treatment.

CONCLUSION

Surgical excision of a keloid followed by immediate, single-fraction, high-dose radiotherapy is both safe and effective in preventing recurrence of therapy-resistant keloids.

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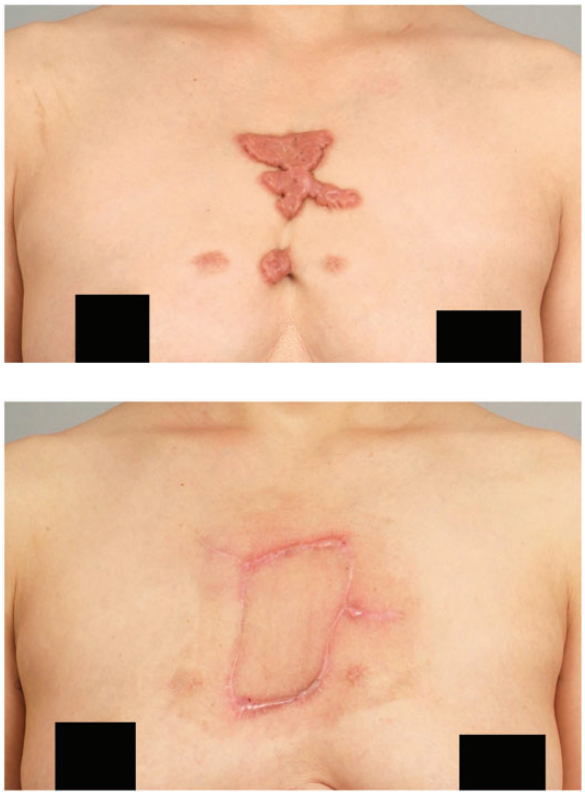

Fig. 5. A case of keloid of the anterior chest wall (**a**) before treatment, and (**b**) 8 months after treatment.

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