Short Communication


Post-keloidectomy Irradiation Using High-dose-rate Superficial Brachytherapy

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Keloid/Postoperative radiotherapy/High-dose-rate radiotherapy/Superficial brachytherapy.

A study was conducted to evaluate the early results of high-dose-rate superficial brachytherapy (HDR-SB) after keloidectomy. Between April 2008 and April 2009, 21 patients with 36 histologically confirmed keloids were treated with postoperative HDR-SB. The tube applicator was placed on the skin to match the area of the surgical wound, and a spacer 5 mm thick was placed between the skin and the applicator. A dose evaluation point was established below 2 mm from skin surface, and 20 Gy was delivered in 4 daily fractions to keloidectomy scars on the anterior chest wall, scapular region, lower jaw and suprapubic region. A dose of 15 Gy was delivered in 3 daily fractions to lesions in other areas. The median follow-up period was 18 months (range, 9 to 29 months). Therapeutic outcome was judged in terms of recurrence, control, or acute side effects. Three keloids (9.7%) in two patients showed local recurrence, with a median time to failure after HDR-SB of 12 months. All recurrences affected the anterior chest wall. Dysraphia occurred in only one patient with an anterior chest wall lesion. Excluding the cases of recurrence, acceptable cosmetic results were achieved. Our results indicate that HDR-SB is effective and safe for preventing recurrence of keloids.

INTRODUCTION

Postoperative irradiation has been established as the most effective treatment for preventing the re-formation of keloids.1,2) External-beam radiotherapy using electron beams and soft X-rays is the most widely employed approach for postoperative irradiation, but from the viewpoint of dose distribution, this is disadvantageous for irradiation of long wounds, or wounds located on an uneven skin surface.

Brachytherapy is an alternative form of radiotherapy for wounds that are difficult to irradiate with an external beam, and many articles have described the use of high-dose-rate (HDR) interstitial brachytherapy3–6) and low-dose-rate (LDR) superficial brachytherapy.7,8) However, HDR interstitial therapy demands a very tight radiation schedule to shorten the applicator implantation period. On the other hand, LDR superficial brachytherapy requires a long time for daily treat-

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METHODS AND MATERIALS

Patient characteristics

Between April 2008 and April 2009, 21 patients with 36 histologically confirmed keloids were treated with postoperative HDR-SB. Sixteen patients (76%) were female, and the remaining 5 (24%) were male. The median age of the patients, who were all of Asian ethnicity, was 41 years (range 18–69 years). The keloids were located on the anterior chest wall, scapular region, lower jaw, suprapubic region, and other areas (Table 1). The median length of surgical wounds was 8.5 cm (range 3.3–28.8 cm). All the patients gave informed consent and agreed to participate in the follow-up investigation.

Treatment

All the surgical wounds were treated by HDR-SB after complete resection of the keloid; large keloid scars that
could not be extirpated in a single operation were excluded. Our surgical procedure has been reported previously.9) HDR-SB was delivered using a remote afterloading system from an Ir-192 source, and was started within 24 hours after surgery. The plastic tube applicator 3 mm thick was placed on the skin to match the surgical wound, and then fixed with adhesive tape. To ensure uniform irradiation of the wound, two or three parallel applicators were used to cover as much of the wound as possible (Fig. 1), and a spacer 5 mm thick was placed between the skin and the applicator. A dose evaluation point was established below 2 mm from skin surface, and 20 Gy was delivered in 4 daily fractions to the anterior chest wall, scapular region, lower jaw and suprapubic region. A dose of 15 Gy was delivered in 3 daily fractions to lesions in other areas.

Follow-up

Patients underwent regular surveillance every month in the first year after completion of radiation therapy, and then every 3 to 6 months thereafter. The median follow-up period was 18 months (range, 9 to 29 months). Therapeutic outcome was judged in terms of recurrent or controlled and acute side effects. Even very small elevations in patients who were otherwise satisfied with the results were considered as recurrences. The items evaluated as acute skin effects were radiation dermatitis (erythema, pruritus), wound complication (dysraphia) and skin pigmentation disorder (hypopigmentation or hyperpigmentation) in the treated area or just around it. Patients were evaluated according to the National Cancer Institute Common Terminology Criteria of Adverse Effects scale (CTCAE) version 3.0.10

RESULTS AND DISCUSSION

Three keloids (9.7%) in two patients showed local recurrence, with a median time to failure after HDR-SB of 12 months. All of these recurrences were observed on the anterior chest wall, and no recurrence was seen elsewhere (Table 1). One of the patients with relapse was a 26-year-old woman who had two keloids on the anterior chest wall (multiple keloids were also present on the bilateral ear lobes but were not treated at the same time). These two keloids were treated by surgery and HDR-SB, and showed relapse four months later. The wound sizes were 6 cm and 10.5 cm. The other patient with relapse was a 34-year-old woman who had

Table 1. Localization of the keloids (n = 36), and the therapeutic results obtained

<table>
<thead>
<tr>
<th>site</th>
<th>No. of patients</th>
<th>controlled</th>
<th>Recurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior chest wall</td>
<td>16</td>
<td>13 (81%)</td>
<td>3</td>
</tr>
<tr>
<td>Scapular region</td>
<td>7</td>
<td>7 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>Lower jaw</td>
<td>6</td>
<td>6 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>Suprapubic region</td>
<td>4</td>
<td>4 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>3 (100%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Fig. 1. Illustrations of applicators and dose distribution. a, b) single tube applicator. c, d) applicator comprising two parallel tubes; the distance between the applicators was 16 mm. The distance between the spacers was altered according to the shape of the wound, and a bolus 5 mm thick was placed between the skin and the applicator when the distance between the spacers exceeded 10 mm. The spacer and bolus were made from a tissue-equivalent solid gel with a density of 1.0 g/cc.
multiple keloids on the chest wall. Two large keloids had already been treated using surgery and electron beam radiotherapy three years before, and two new lesions located near the previously treated area were treated by surgery and HDR-SB on this occasion. The wound sizes were 5 cm and 12.5 cm. The longer lesion was sutured again after radiotherapy because of dysraphia, and relapse occurred in the resutured region 12 months after completion of postoperative radiotherapy.

Although transient erythema occurred in almost all patients a few weeks after radiotherapy, there was no incidence of > grade 2 toxicity or other side effects such as changes in skin pigmentation. Dysraphia occurred in only one patient with an anterior chest wall keloid, but suture diastasis had already been confirmed before the start of radiotherapy. Excluding the cases of recurrence, acceptable cosmetic results were achieved (Fig. 2).

Our present series showed that HDR-SB achieved a high local control rate that did not differ significantly from that achieved by electron beam radiotherapy in a series we reported previously (3/36 vs. 17/121, p = 0.366 by chi-squared test). It was noteworthy that none of the patients developed local recurrence of lesions in the lower jaw or scapular region, which are difficult to treat using external-beam radiotherapy. Electron beam radiotherapy has been performed conventionally, and this reduces the exposure of deeply located normal tissue. However, with electron beam radiotherapy, it is difficult to administer a uniform radiation dose to wounds that are located on an uneven skin surface because of variations in the distance between the skin surface and the radiation source. By applying the applicator closely to the skin, HDR-SB can supply a uniform radiation dose even if a wound is seated in an uneven skin surface. This makes it especially useful for wounds in the skin of the lower jaw, shoulder, chest wall and axilla.

In this series, HDR brachytherapy was performed using the superficial mold irradiation technique, which has been described in only one previous report detailing its use for prevention of keloids. Although the median length of the surgical wounds treated in the present study was double that in other reports (8.5 cm vs. < 4.2 cm), the local control rate was almost equal to that reported previously for HDR interstitial brachytherapy (recurrence rate 9.7% vs. 3.5–12.5%). As keloid size has been proven to be a prognostic factor, these results suggest that the efficacy of HDR-SB is comparable or superior to that of HDR interstitial brachytherapy.

The advantage of the HDR-SB technique is that the applicator can be used as occasion demands. Treatment using a detachable applicator has certain advantages, one of which is extension of the total treatment period. Prolongation of the implantation period during HDR interstitial therapy causes wound dehiscence and keloid recurrence in the insertion area, and therefore this form of treatment requires a very tight schedule, e.g., patients undergoing radiotherapy six times over a two-day period in the series reported by Guix et al. Such a schedule is considerably demanding for medical staff, and moreover imposes real hardship on patients with severe pain, who need to come to the treatment room frequently. A general radiation schedule performed once a day is compatible with our present technique, thus reducing the degree of stress for both patients and staff.
The other advantage of the HDR-SB technique is its flexibility in adaption to the shape of the surgical wound. The shapes and lengths of surgical wounds often change due to cutaneous edema and subcutaneous hematoma. In the tube implantation method, these changes may cause sagging of the tube, resulting in under- or overdosage.\(^7,14-16\) Using HDR-SB, the distance between the source and the skin can be kept constant by attaching the applicator at every treatment. Furthermore, surgical wounds that are very long or irregularly curvilinear, which are difficult to treated using HDR interstitial brachytherapy, can be treated easily by HDR-SB.

The disadvantage of HDR-SB is that the area of exposure, including normal tissue, is a little wider than that for HDR interstitial brachytherapy because of the longer source-target distance setting (5 mm vs. 7–8.5 mm)\(^3,17\) In the present series, no patients experienced toxicity of grade 3 or more. Although dysraphia occurred in one patient, this might not have been caused by the irradiation but by the suturing technique employed, judging from the postoperative course.

The irradiation doses that we employed were based on the results obtained with electron beam radiotherapy at our institution.\(^9,11\) Our regimen was based on a concept of 20 Gy delivered in 4 daily fractions to sites with high stretch tension, 10 Gy delivered in 2 daily fractions to sites with low stretch tension, and 15 Gy delivered in 3 daily fractions to lesions in other areas. Kal and Veen\(^6\) reviewed the literature pertaining to the results of postoperative irradiation therapy and observed that the optimal irradiation regimen was one that delivered a biologically effective dose (BED) of over 30 Gy, equivalent to over 18 Gy delivered in 3 daily fractions, or to over 20 Gy delivered in 4 daily fractions. This suggests that the doses applied postoperatively in our treatment regimens were not excessive. Although high-dose irradiation may decrease the degree local recurrence, it may also increase the incidence of adverse events. Treatment of keloid, which is essentially a cosmetic procedure, should not place a patient at risk of irreversible side effects, even if local recurrence is successfully prevented. Therefore, we consider that our regimens employ an optimum dose setting that can deliver benefits to most patients with minimal side effects.

The present results suggest that HDR-SB can be performed without any serious cosmetic sequelae. However, our follow-up period was too short to allow evaluation of any late toxicity such as secondary malignancy, and it must be borne in mind that the lesions treated were benign, so that a longer follow-up will be needed to further confirm the safety of HDR-SB.

REFERENCES