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Reconstructive

Z-plasty and Postoperative Radiotherapy for Upper-arm Keloids: An Analysis of 38 Patients

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Background: Therapies for upper arm keloids include surgical excision followed by postoperative radiotherapy, silicone tape stabilization, and steroid plaster. However, a universally accepted therapeutic strategy for upper-arm keloids is lacking.

Methods: All consecutive patients with single upper-arm keloids who underwent keloid excision followed by tension-reducing suturing, multiple z-plasties, and postoperative radiotherapy in 2013–2016 in the keloid/scar specialist clinic at the Department of Plastic, Reconstructive and Aesthetic Surgery of Nippon Medical School, were included in this case series study. Only keloids that arose from the small injury produced during Bacillus Calmette–Guérin vaccination were selected. The postsurgical radiotherapy regimen was 18 Gy administered in 3 fractions over 3 days. Radiotherapy was followed by tension-reducing wound self-management with silicone tape and, if needed, steroid plaster. The primary study objective was keloid recurrence during the 24-month follow-up period. Recurrence was defined as the growth of stiff red lesions in even small areas of the scar that was refractory to at least 2 months of steroid plaster therapy.

Results: In total, 38 patients with 38 lesions were enrolled. Two lesions (5.3%) recurred. Both recurrences were successfully treated by concomitant steroid plaster and steroid injection. The recurrence patients were significantly more likely than the nonrecurrence patients to have multiple keloids. The 2 groups did not differ in terms of original keloid size.

Conclusions: Upper-arm keloids can be successfully treated by customized plans that involve appropriate surgical modalities (including multiple z-plasties), postoperative radiotherapy (18 Gy/3 fractions/3 d), and postoperative wound/scar self-management with silicone tape and steroid plaster. *(Plast Reconstr Surg Glob Open 2019;7:e2496; doi: 10.1097/GOX.0000000000002496; Published online 28 November 2019.)*

INTRODUCTION

Keloids are the result of prolonged and intense dermal inflammation that is driven by genetics, systemic factors such as high cytokine levels, and local factors such as infection and sustained mechanical loading.[1–5] We showed previously that approximately 5% of all keloids develop on the upper arm.[6] These keloids are largely driven by 2 etiological factors. First, the upper arm is the most common site of Bacillus Calmette–Guérin (BCG) vaccination; it is also prone to acne or folliculitis, which are well-known triggers of keloidogenesis.[7] All of these triggers arouse an inflammatory response. Second, the upper arm is subject to considerable skin tension due to the frequent movements of the shoulder and elbow joints.[6] These movements cyclically stretch the skin of the upper arm in the longitudinal direction. Arm growth during childhood also imparts continuous stretching tension. This mechanical tension on even a minor upper arm wound caused by vaccination or acne/folliculitis exacerbates and prolongs the reticular dermal inflammation in the wound.[6,8,9] This scenario explains why highly mobile anatomical sites are in general prone to keloid formation.[6,8] The resulting inability to progress through the first (inflammatory) phase of wound healing in a timely fashion is a well-known cause of keloidogenesis.[1,8,9]

The most widely used treatments for upper arm keloids are surgical excision with postoperative radiotherapy, steroid injection, sheeting, pressure therapy, and laser therapy.[10–12] However, an established and widely used treatment strategy for these keloids is lacking. We have

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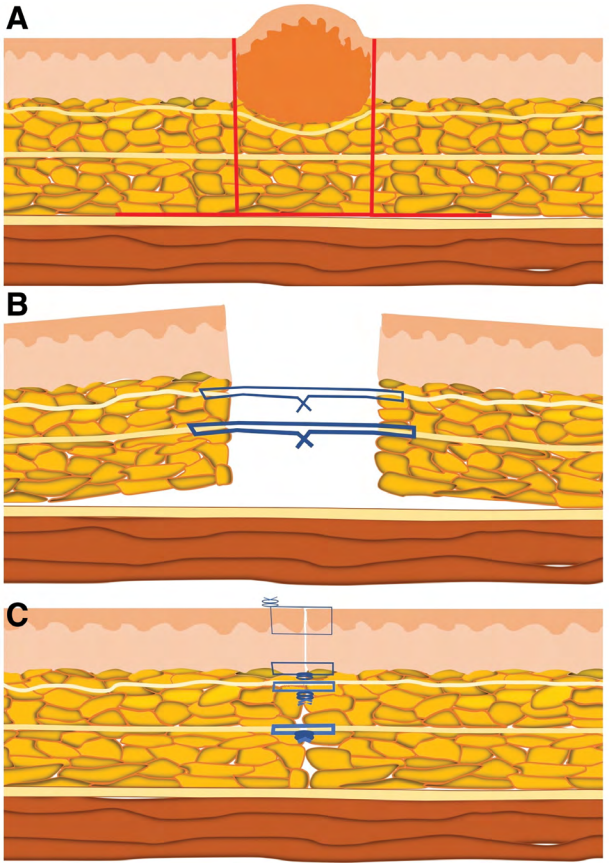

Fig. 1. Schematic depiction of the multiple layers of sutures that are used to close the wound after excision of an upper-arm keloid. Because keloids grow from the reticular dermis, it is important to disrupt the tension on the dermis after keloid excision. This can be largely achieved by applying deep sutures on the fibrous membrane in the fatty tissue: this causes the upper tissues on either side of the wound to juxtapose each other naturally. Dermal sutures should never be applied to force the dermal tissues together. A, The red lines indicate the excision and undermining lines. B, The view after the fatty tissues under the keloid is removed, the tissue above the deep fascia is undermined, and the fibrous membranes deep in the fatty tissue and just below the subdermal vascular network are sutured using PDSII thread. C, The view after the superficial fasciae, the fibrous membrane just below the dermis, the dermis, and the superficial layer are sutured.

developed a combination treatment strategy for these keloids. To determine its effectiveness, we analyzed all small- to medium-sized upper-arm keloid cases that were treated with this strategy in our facility in 2013–2016. We show here that this approach is highly effective for these keloids.

METHODS

Ethics Statement

This case series study was performed after obtaining approval from the Ethics Committee of Nippon Medical School Hospital. The requirement to obtain patient consent was waived due to the retrospective nature of the study.

Patient Selection

A retrospective medical chart review identified all consecutive adult patients with upper-arm keloids who (1) underwent keloidectomy in 2013–2016 in the outpatient clinic of the keloid/scar specialist clinic in the Department of Plastic, Reconstructive and Aesthetic Surgery, Nippon Medical School (Tokyo, Japan) and (2) were followed up for at least 24 months. All patients with a single upper-arm keloid that arose from BCG vaccination and underwent complete excision, tension-reducing suturing, and multiple z-plasties followed by the postoperative radiation and wound self-management protocol described below were selected from this group. Patients with upper-arm keloids that arose from major traumatic or artificial injuries (eg, orthopedic surgery) were excluded. Keloid was defined as a continually growing elevated red scar whereas hypertrophic scar was defined as a hard, mildly elevated scar with limited growth. Patients with hypertrophic scars were excluded along with patients with multiple upper-arm keloids that were treated by conservative therapies, partial resection, or flap surgery.

Surgical and Postoperative Radiation Treatment Protocol

All study patients were treated with a protocol consisting of complete excision, tension-reducing suturing, Z-plasty, postoperative adjuvant radiotherapy, and postsurgical wound self-management.

Before surgery, the patient was placed under general anesthesia. The keloid was completely excised along with a minimal normal skin margin and all fatty tissues under the keloid. Thus, all tissues above the deep fascia of the deltoid, brachialis, triceps, or biceps brachii muscle were removed. To reduce the risk of recurrence, subcutaneous/fascial tension-reducing sutures (Fig. 1) and z-plasties were employed for wound closure. Briefly, the wound edges were undermined just above the deep fascia and the deep fibrous membrane in the fatty tissue above the deep fascia (ie, the superficial fascia) was sutured using 0 or 2-0 polydioxanone sutures (PDSII; Ethicon, Inc., Somerville, NJ). The fibrous membrane in the fatty tissues just below the subdermal vascular network was then sutured using 3-0 PDSII. This suturing protocol smoothly elevates the wound edges so that they juxtapose each other naturally. Consequently, there is little tension on the dermis, which is where keloidogenic inflammation starts and proceeds.[8,9,13]

Z-plasties were then designed. The sides of each triangular flap were 7–10 mm long. Depending on total wound length after excision, the pitch between each Z-plasty was 2–4 cm.[14] In our experience, this pitch has the best outcomes (personal observations). However, studies on this issue are warranted. After confirming that the triangular flaps were fully elevated and could be easily transposed with each other, the dermis was closed with 4-0 PDSII sutures. Superficial sutures with 6-0 polypropylene (Prolene; Ethicon) were then added.

In some cases, the keloid had an uneven, zigzag shape, which allowed us to apply the natural w-plasty with triangular skin flaps instead of Z-plasties.

All patients underwent postoperative radiotherapy with a 4-MeV electron beam that delivered a total radiation

dose of 18 Gy in 3 fractions over 3 days. Surgery was conducted on a Wednesday or Friday. If surgery occurred on Wednesday, radiotherapy was performed on the following Thursday, Friday, and Monday. If surgery was performed on Friday, radiotherapy was administered on the following Monday, Tuesday, and Wednesday.

The sutures were removed 7–14 days after surgery depending on the patient's availability.

After suture removal, all patients were asked to fix their wound/scar for 24 hours/d with silicone tape (Mepitac; Mölnlycke Health Care, Gothenburg, Sweden) for more than 6 months. The patient was informed that this would limit the external mechanical forces on the wound that could otherwise provoke keloid recurrence. The patients were advised to leave the tape attached (including during washing) until it fell off and then to apply a fresh tape.

Patient Follow-up and Additional Therapies

All patients visited the outpatient clinic 3 months post surgery and every 2–6 months thereafter. Total follow-up duration was more than 24 months. If the postoperative scar exhibited stiffness with redness in even small areas, anti-inflammatory steroid plaster (Eclar plaster; Hisamitsu Pharmaceutical Co., Inc., Tokyo, Japan) was administered instead of silicone tape.[11] The patient was asked to change the plaster daily. It was planned that if the stiffness and redness had disappeared at the next visit 2–6 months later, the steroid plaster would be replaced with heparinoid ointment (Hirudoid Soft Ointment; Maruho Co., Inc., Osaka, Japan) to keep the scar surface moist. However, if the steroid plaster could not eliminate the stiffness/redness in 2–6 months, the lesion was considered to have recurred and steroid injection was added to steroid plaster administration, even if the refractory area was tiny. The steroid injection involved a single injection via a 30-G needle of 1–2 ml of 5-mg triamcinolone acetonide (Kenacort; Bristol-Myers Squibb K.K., Tokyo, Japan) diluted with 1% lidocaine.

Primary Study Outcome and Other Variables

The primary outcome was recurrence in the 24-month follow-up period, defined as stiffness with redness in even tiny areas of the postoperative scar that were refractory to 2–6 months of steroid tape treatment. Other variables were original keloid size, presence of postoperative complications (eg, wound dehiscence, pigmentation, depigmentation, or telangiectasia), whether silicone tape was replaced with steroid plaster, duration of silicone tape and steroid plaster use, number of steroid injections before recurrence disappearance was observed, the postoperative durations to lesion recurrence and scar maturation (defined as scars lacking redness), and scar width at 24 months.

Statistics

All variables were expressed as means or frequency. Groups were compared by using Student's t test or Chi-squared test. All statistical analyses were performed by using Microsoft Excel 97–2003 (Microsoft, USA) and SPSS statistical software (SPSS, Chicago, IL, USA). P values of <0.05 were considered to indicate statistically significant differences.

RESULTS

The study included 38 lesions on 38 consecutive patients. The mean age of the patients was 34.2 years. Two and 36 were male and female, respectively. Ten patients also had keloids on other body sites. Of the 38 lesions, 10 (26.3%) and 28 (73.7%) were ≤10 cm and >10 cm in diameter, respectively.

Of the 38 postoperative scars, 2 (5.3%) exhibited small areas of stiffness at 3 postoperative months. In these cases, steroid plaster replaced the silicone tape. Five and 7 months after surgery (ie, 2 and 4 months after starting steroid tape therapy, respectively), the stiffness had not resolved. Thus, the lesions were considered to be recurrences and a single 5-mg triamcinolone acetonide injection was immediately administered. Steroid tape administration was continued for another 6 and 9 months, respectively. At that point (ie, 11 and 16 months after surgery, respectively, and 8 and 13 months after starting steroid tape treatment, respectively), the lesions had vanished and the steroid tape was replaced with heparinoid ointment. Thus, the recurrence rate in our series was 5.3% (2 out of 38 lesions), and the average postoperative duration to steroid tape-resistant recurrence was 3 months.

Both patients with recurrences were female and had keloids on other body sites. The recurrence patients were significantly more likely than the nonrecurrence group to have multiple keloids (20% versus 0%, $P = 0.015$). The 2 groups were similar in terms of sex ratio (100% versus. 94.4% females, $P = 0.739$) and preoperative keloid size (12.0 versus 11.2 cm, $P = 0.5$).

The postoperative scar width at 24 months ranged from 1 to 3 mm (Figs. 2–5). The scars tended to be wider on the edge of the z-plasties and at some points of the w-plasties (Figs. 4 and 5).

Postoperative complications consisted of pigmentation on the irradiated area in 1 case (2.6%) 3 months after surgery; it improved spontaneously over the next 12 months. Two cases (5.3%) exhibited telangiectasia 24 months after surgery that was treated by long-pulsed Nd:YAG laser. There were no cases of depigmentation or wound dehiscence after radiotherapy. All mature scars were soft and white (Figs. 2–5).

DISCUSSION

Our current keloid therapy protocol consists of excision followed by tension-reducing suturing, Z-plasty, postoperative radiotherapy, and postoperative wound self-care. The present study of 38 cases of small- to medium-sized upper-arm keloids showed that this protocol had excellent outcomes: the recurrence rate was only 5.3%. In addition, these recurrences involved very small lesions that were readily and completely extinguished by our rapid implementation of steroid tape and injection. These good results are notable given that keloids have very high recurrence rates after excision alone (range, 45%–100%).[15]

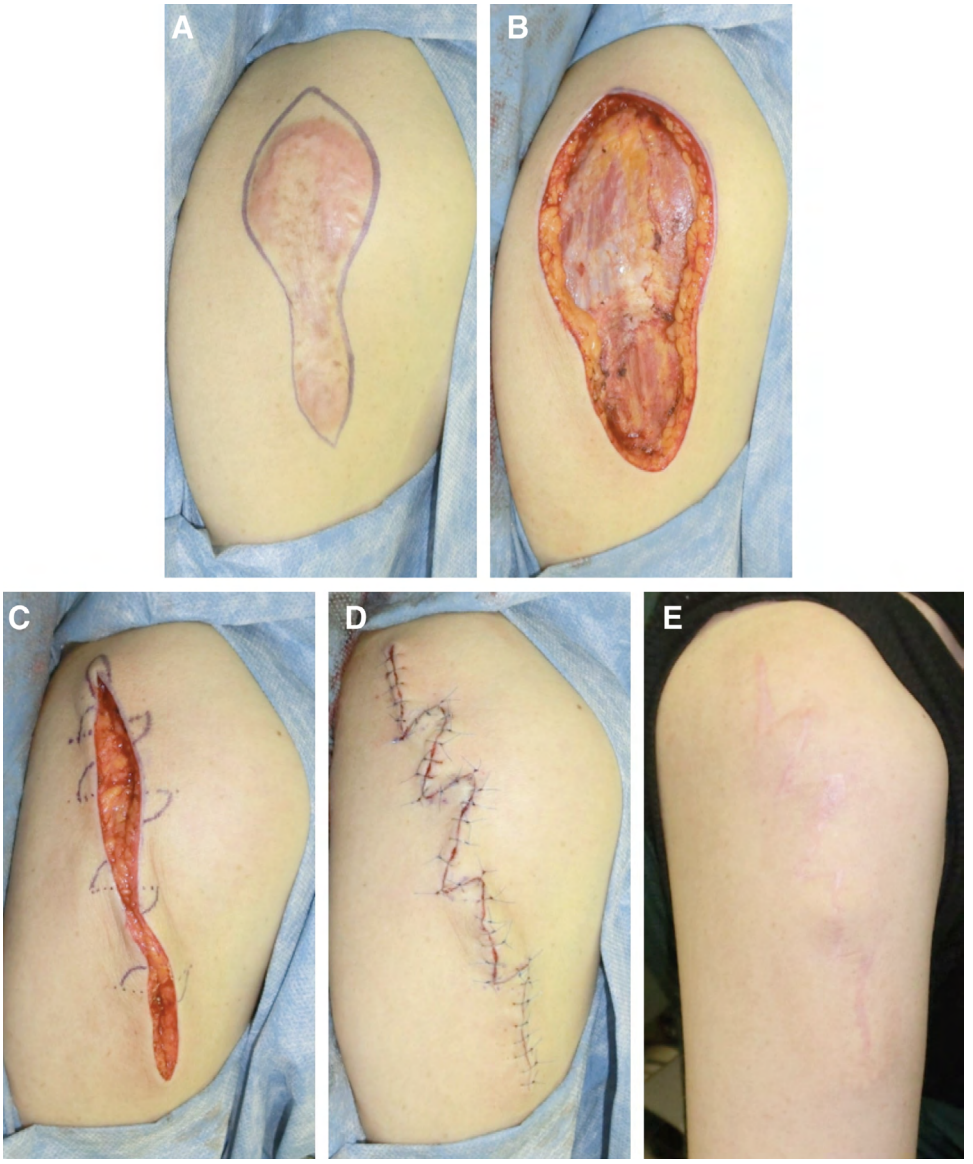

Fig. 2. The case of a 39-year-old woman with an upper-arm keloid. A, Preoperative view. B, Immediately after excision. C, Immediately after superficial fascial suturing and the design of the z-plasties. D, Immediately after the operation. E, Two years after the operation.

Characteristics of Upper-arm Keloids

The upper arm is prone to keloid formation because the BCG vaccine is usually injected intradermally in the upper arm: this vaccine is known to induce strong inflammatory responses in all skin layers.[16] The inflammatory effect of this vaccine can then be augmented by another key etiological factor that strongly affects the upper arm, namely the movements of the shoulder and elbow joints, which predominantly impose a marked unidirectional mechanical tension on the skin that runs along the long axis of the upper arm. This mechanical tension also explains why shoulder keloids grow down from the shoulder toward the elbow. The intersecting pro-inflammatory effects of BCG vaccination and mechanical tension may be more common in Japan than other countries because although the BCG vaccine is now generally given around 6 months in Japan, many children used to receive it later in childhood.[17,18] Given that older children are substantially more mobile than infants, it is possible that these later vaccination sites are subjected to more mechanical tension and therefore are at greater risk of keloidogenesis.

Surgical Tips and Pitfalls Relating to Upper-arm Keloids

A key concept in scar excision surgery is the importance of disrupting the postoperative vertical tension on the dermis (ie, tension that travels upward to the dermal layer from muscle and bone movements). This is because the dermis is where keloidogenic inflammation starts and progresses.[13,19] A key way to achieve this tension disruption is by placing sutures in the fibrous membrane of the fatty tissue (ie, superficial fascial sutures). Depending on the extent of excision, sutures are also sometimes placed in

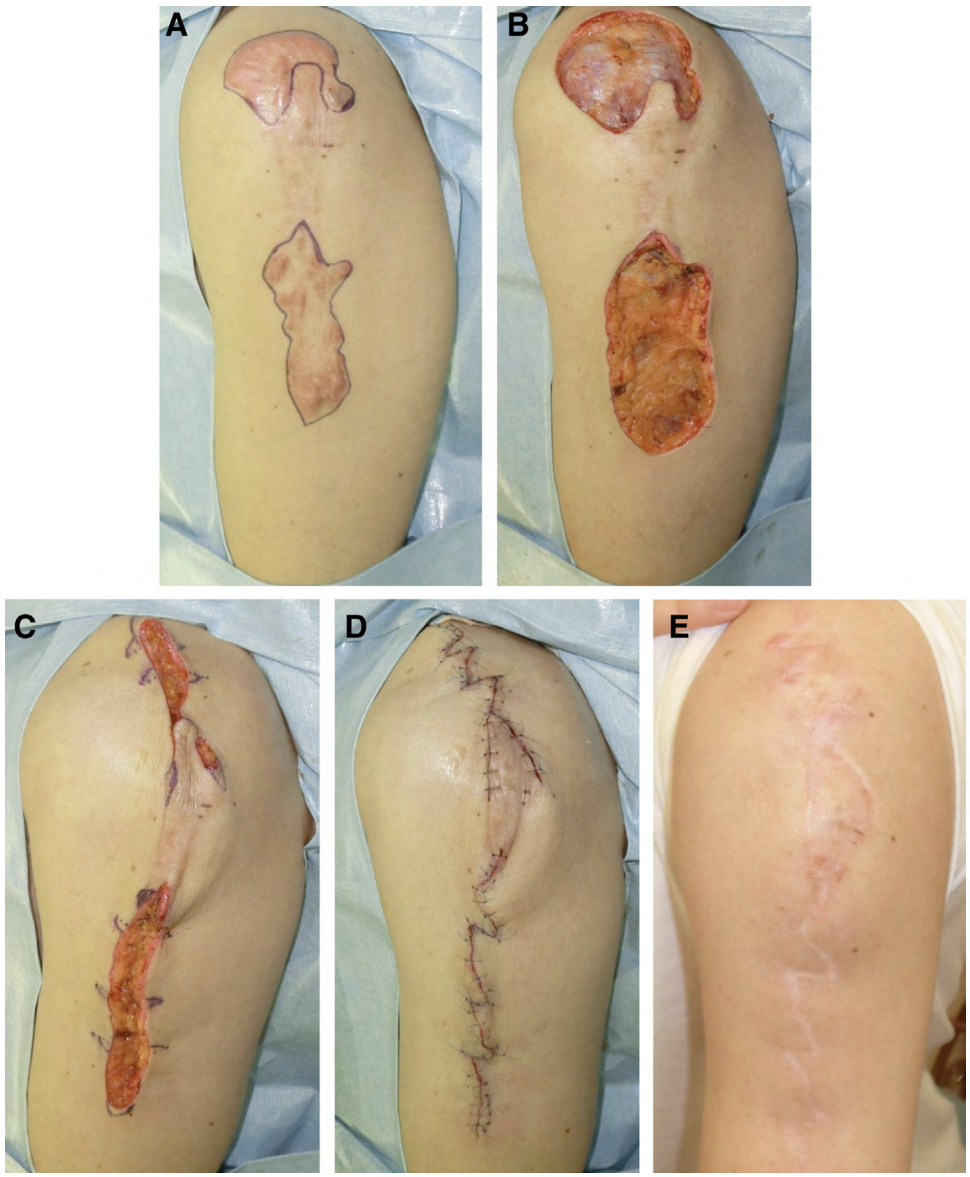

Fig. 3. The case of a 46-year-old woman with an upper-arm keloid. A, Preoperative view. The central mature scar of the keloid was left untouched. B, Immediately after excision. C, Immediately after superficial fascial suturing and the design of the z-plasties. D, Immediately after the operation. E, Two years after the operation.

the deep fascia (ie, deep fascial sutures). Their effect is to absorb the impact of mechanical stress from the movements of the muscles and joints in the body area and thus spare the dermis from this stress.[13] However, it should be noted that deep fascial sutures can be neuropathic in the upper arm (personal observations). Therefore, their use should be limited. Consequently, we generally only use superficial fascial sutures after upper-arm keloid excision. These sutures are applied every 2–3 cm along the wound bed and involve placing the suture through the fibrous membrane approximately 1–2 cm away from the wound edge while avoiding inclusion of soft fatty tissue as much as possible (Fig. 1). Thereafter, sutures are placed in the fibrous membrane that lies just below the dermis. These sutures are inserted into the membrane 0.5–1 cm away from the wound edge and reinforce the fascial suturing. One can be sure that adequate tension reduction below the dermis has been achieved when the wound edges naturally and softly juxtapose each other before the dermal sutures are placed. In our opinion, this concept is key to preventing pathological scar formation after surgery.

Because upper-arm keloids always grow along the long axis of the arm, excision surgery tends to leave a long scar that runs parallel to the same axis and is prone to contracture. Therefore, it is also essential to disrupt the mechanical tension pulling horizontally on the linear scar. To achieve this, we use multiple z-plasties that are spaced every 2–4 cm.[14,20] Notably, sometimes the

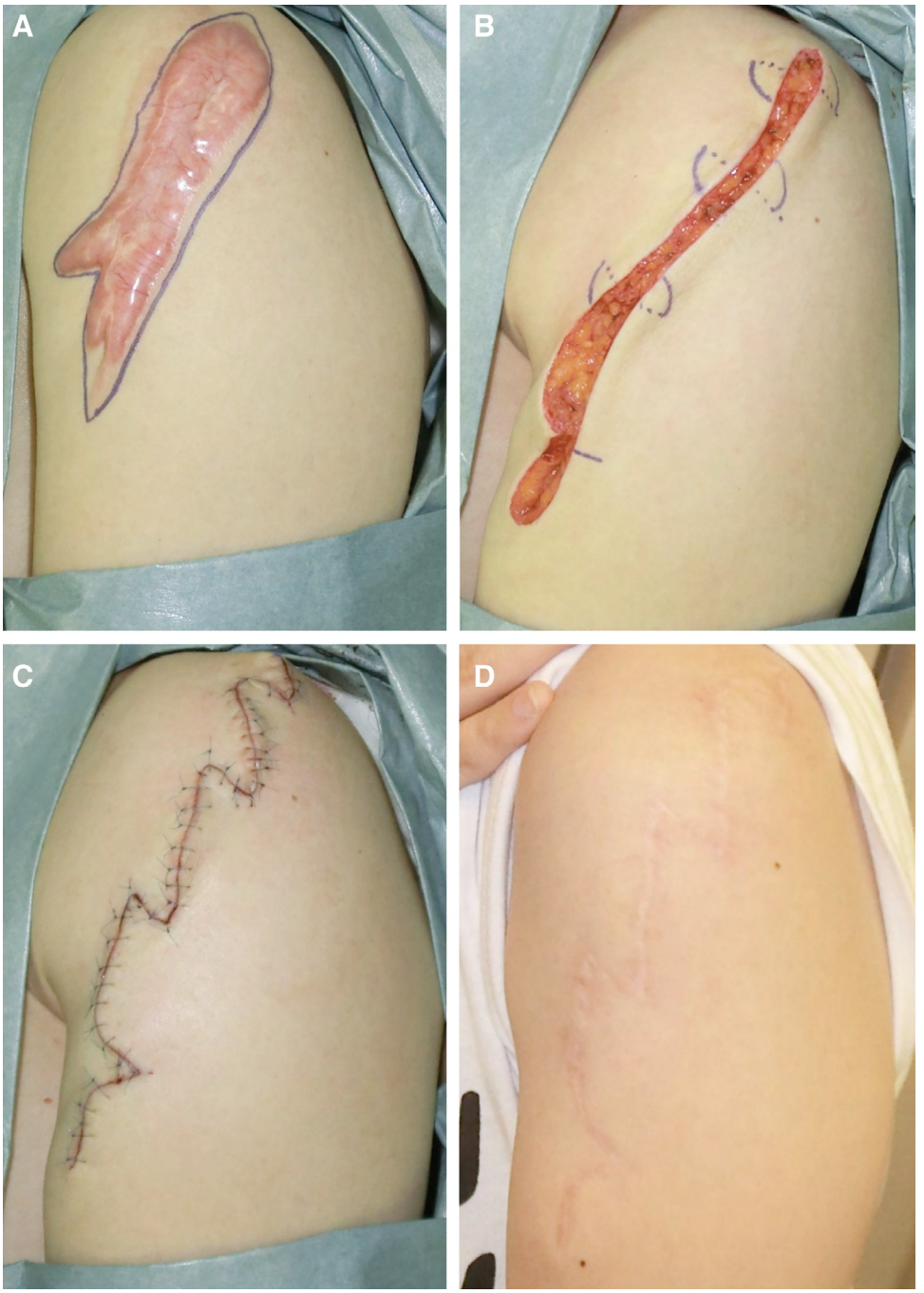

Fig. 4. The case of a 32-year-old woman with an upper-arm keloid. A, Preoperative view of the scar and the design used to excise the keloid with a minimal margin so that a natural w-plasty could be applied. B, Immediately after superficial fascial suturing and the design of the z-plasties and a natural w-plasty. C, Immediately after the operation. D, Two years after the operation.

wound has an uneven edge after excision that allows us to apply a natural w-plasty instead of Z-plasties (Figs. 4 and 5). Both plasty types disrupt the mechanical tension on the wound.

Postoperative Radiotherapy

Because postoperative external radiotherapy is the most effective therapy for preventing keloid recurrence after keloidectomy,[19,21,22] it plays a key role in our keloid treatment protocol. This therapy has an almost century-long history as a treatment for abnormal scars.[23] Multiple variants involving x-rays (superficial or orthovoltage), β-rays (electron beams, 32P, or $^{90}Sr/^{90}Y$), and γ-rays (^{60}Co or ^{192}Ir) directed via teletherapy or brachytherapy modalities (contact, high-dose rate superficial, or low-dose rate superficial) have been reported.[24]

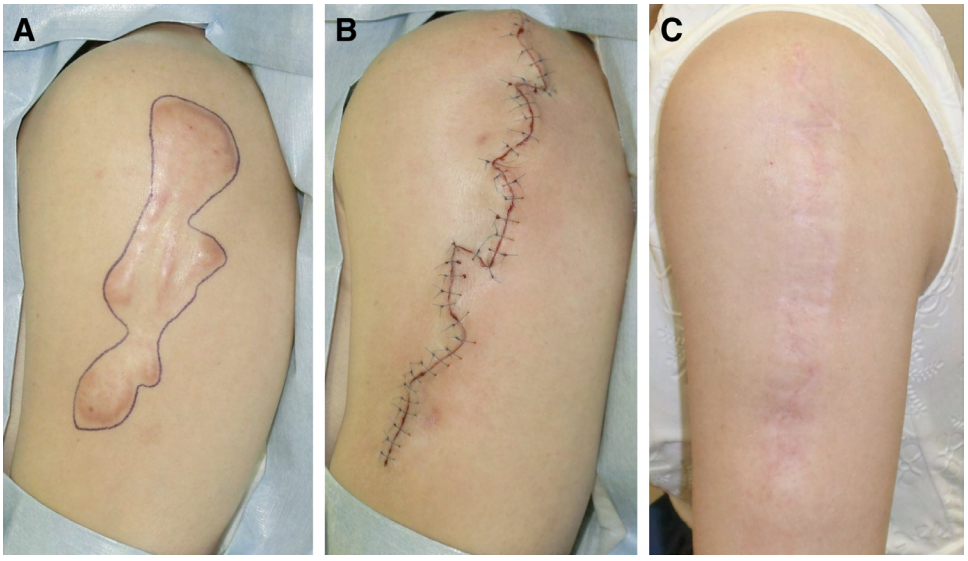

Fig. 5. The case of a 34-year-old woman with an upper-arm keloid. A, Preoperative view of the scar and the design used to excise the keloid so that natural w-plasties could be applied. B, Immediately after the operation. C, Two years after the operation.

Because keloids on different body sites vary in their predilection toward postoperative recurrence, we employ site-specific postkeloidectomy radiotherapy regimens in our institute. For upper-arm keloids (ie, the lesion extends below the shoulder), the regimen consists of a 4-MeV electron beam at a total dose of 18 Gy given in 3 fractions over 3 consecutive/semiconsecutive days starting 1–3 days after surgery. If the intrinsic radiosensitivity and repair capability (ie, the α/β ratio) of keloids is set at 10, this regimen yields a biologically effective dose of 28.8 Gy.[25,26] Full shielding to protect the normal tissues is applied.[19] The present study showed that this approach (combined with several other approaches) associated with a low recurrence rate of 5.3%. This contrasts with a recurrence rate of 26.7% when we subjected excised upper-arm keloid wounds to a 15 Gy/3 fractions/3 d regimen in 1998–2000.[27] Our current radiotherapy protocol also did not induce complications such as surgical wound dehiscence, permanent pigmentation, depigmentation, or radiation dermatitis. Moreover, although it has been suggested that postoperative radiotherapy may associate with carcinogenesis,[28] we did not observe any secondary carcinogenesis cases during the follow-up period, which was at least 24 months and extended to 6 years in some cases. Moreover, malignant tumors associated with modern postoperative radiotherapy protocols have not yet been reported.[24] Nevertheless, we are continually striving to further reduce the radiation dose by developing new surgical methods and irradiation modalities. It should be noted that the 2 patients who exhibited recurrence in the present study also had keloids on other body sites. This suggests that the recurrence rate is high in multiple keloid cases. Therefore, it may be possible to further reduce the radiotherapy dose by factoring in keloid-related factors (eg, keloid number) that associate with high recurrence rates.

Postoperative Scar Management

To further limit external mechanical forces on the wound/scar after keloid excision, the postoperative scars in our clinic are routinely self-treated with silicone tape fixation for at least 6 months after suture removal. The patients are also encouraged to avoid lying on the affected part during sleep and to temporarily discontinue silicone tape fixation and apply an antibiotic ointment if acne or folliculitis lesions arise near the scar.

Despite the use of tension-reducing operative methods, radiotherapy, and the assiduous postoperative application of tension-reducing silicone tape fixation, we sometimes have cases in which the postoperative scar evinces small areas of stiffness with redness. Because this indicates inflammation and can be a harbinger of keloid recurrence, the silicone tape therapy in these cases is immediately replaced with daily steroid plaster application (alternatively, steroid plaster can be placed on the stiff area under the silicone tape). This treatment is readily self-administered. If the steroid plaster does not improve the stiffness of the scar within several months, the scar is injected with steroid (triamcinolone acetonide).[15,29] As shown by the 2 cases that exhibited small regions of scar stiffness in our study, this salvage therapy has excellent long-term outcomes.

It should be noted that we can employ this strategy because Japanese physicians have commercial access to a higher-potency steroid (20 $\mu g/cm^2$ deprodone propionate) plaster that effectively treats keloids as well as abnormal postoperative scarring (including stiff scars).[11] By contrast, the only commercially available steroid plasters in the United States and the United Kingdom contain medium-strength steroids (4-$\mu g/cm^2$ fluradrenolide or fludroxycortide). In this case, it may be necessary to consider administering steroid injections immediately after stiffness is observed. Other therapies,

including laser therapy, cryotherapy, and injections with other drugs such as 5-fluorouracil and immunosuppressants, may also help to dampen postoperative scar inflammation.[10,12,29,30]

Thus, tension-reducing surgical methods and radiotherapy must be combined with careful postoperative scar self-management and close follow-up to ensure that any recrudescences are rapidly extinguished.

CONCLUSIONS

There is currently no universally accepted combination treatment algorithm for upper-arm keloids. The present study showed that these lesions can be successfully treated by body site-customized plans that involve appropriate surgical modalities (including multiple z-plasties) followed by postoperative radiotherapy (18 Gy in 3 fractions over 3 days) and scar self-management with silicone tape and steroid plaster. The safety of our radiotherapy regimen will be carefully assessed by attentive surveillance of our expanding case series.

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