Prevention and Management of Keloid Scars

Monica A. Lutgendorf, MD, Elizabeth M. Adriano, MD, and Bruce J. Taylor, MD

A 31-year-old woman, gravida 3, para 2, at 30 weeks of gestation was referred to our institution with the symptom of rapid growth of her keloid scars during her current pregnancy. She was black and had a surgical history of a cesarean delivery and a right vulvar excision for a benign inclusion cyst. The keloid scarring was present at her Pfannenstiel incision and also at the site of her right vulvar excision. The scarring was cosmetically disfiguring and physically painful (Fig. 1).

At the time of her repeat cesarean delivery, the keloid scars were excised with assistance from the plastic surgery team (Fig. 2). Immediately after surgery, she was treated by radiation oncology with four daily fractions of radiation therapy. The first dose was administered on the day of surgery to limit risk of recurrence. The radiation therapy consisted of 450–500 cGy fractions with a 1- to 2-cm margin, using 6–9 MeV electrons and appropriate bolus material to ensure adequate dose from skin to depth. The patient did well and was discharged after 4 days.

Her postoperative course was uncomplicated and she had good wound healing with no recurrence of the keloids at her 15-month postoperative visit (Fig. 3). The patient also had a left preauricular keloid that was excised by plastic surgery 8 months after her delivery, and it was also treated with adjuvant external beam radiation therapy with good cosmetic result.

QUESTIONS FOR COMMENTARY

How Often Does Keloid Scarring Occur After Surgery?

The term keloid originates from the Greek word chele, which means “crab claw,” and was first used by Jean Louis Alibert in 1806 to describe extensions of scar tissue into surrounding skin.1 The incidence of keloids and hypertrophic scars is affected by disruption of the dermis and underlying tissue, with keloid formation after surgery ranging between 40% and 70% and up to 91% after burn injury.2,3 Keloids are also more common in individuals with darker skin, affecting 4.5% to 16% of blacks and Hispanics. The peak incidence is in individuals between 10 and 30 years of age.3

What Causes Keloid Formation? What are the Risk Factors for Keloid Formation?

Although the exact etiology of keloid scarring remains elusive, several mechanisms have been proposed. There is an abnormal proliferation of fibroblast cells, which may be caused by increased growth factor activity (transforming growth factor-beta and platelet-derived growth factor), as well as high levels of collagen, elastin, proteoglycan, and fibronectin in the extracellular matrix.4,5 These abnormal proteoglycans cause the formation of a disorganized extracellular matrix and collagen architecture.5 The abnormal proliferation of fibroblasts may be attributable to abnormal keratinocyte regulation of the fibroblast cells1 or from a primary derangement of the fibroblast cell.

There is also an increased ratio of type I to type III collagen and a defect in the downregulation of type I collagen synthesis.6 Additionally, lower rates of apoptosis are seen in keloid fibroblasts. Keloids have a decreased activity of the membrane metalloproteinases, which increase matrix breakdown, and elevated levels of collegenase inhibitors, which prevent the breakdown of collagen.5,6 Keloids may also arise from an immune reaction to sebum, because keloids occur more commonly on areas of the body with high concentrations of sebaceous glands, such as the chest wall, shoulder, and pubic area, and are rare on the palms and soles, which lack sebaceous glands.5

Several risk factors exist, including operative risk factors such as mechanical forces and tension on surgical wounds, location of the wound, wound infections, and foreign body reactions. Patient-related risk...
factors include ethnicity (skin with darker pigment) and a familial predisposition to keloid scarring.7

What is the Differential Diagnosis for Keloid Scars?
Keloid scars are clinically different from hypertrophic scars; however, it can be difficult to distinguish between the two in the clinical setting. A hypertrophic scar is a fibroproliferative disorder that does not extend beyond the boundaries of the original wound, whereas a keloid is a fibroproliferative disorder that grows beyond the boundaries of the original wound or has an unrecognized origin.7 The main differences between hypertrophic scars and keloids are shown in Table 1.

The differential diagnosis of keloid scars includes hypertrophic scars, infections, chronic folliculitis, keloidal granulomas, dermatofibromas, and malignant tumors such as dermatofibrosarcoma protuberans, and giant cell fibroblastomas.7,9 Biopsies should be considered in anomalous cases and when scarring becomes more severe. It is also important to exclude infections and malignancies before treatment with corticosteroid injections. Additionally, it may be difficult to differentiate tumors in black patients because the color of their scars and tumors may be similar.9

Are Keloids Predictive of Postsurgical Intraabdominal Adhesions?
Postsurgical adhesions were evaluated in a prospective study of 429 women undergoing repeat cesarean delivery. Consistent with reported racial differences in keloid formation, the authors found keloid scarring in 0.5% of whites, 1.6% of Hispanics, 5.2% of Asians, and 7.1% of blacks. Patients with keloids had more dense intraabdominal adhesions between the uterus and the bladder and between the uterus and the anterior abdominal wall.10

Are There Any Intraoperative Surgical Techniques That Can Reduce Keloid Scar Formation?
Prevention of keloids is important because they are notoriously difficult to treat once they develop.5 Meticulous surgical technique can reduce the formation of keloids and hypertrophic scars; however, it cannot prevent all cases. Incisions should be made so that they follow skin creases and avoid incisions that cross joints whenever possible.11 Principles of effective wound repair include the use of atraumatic surgical technique, effective hemostasis, and wound closure with eversion of skin edges. It is also important to adequately debride contaminated wounds, keep wounds clean, and avoid infections. Limiting contact with foreign bodies and using monofilament sutures.
when possible will also decrease the risk of aberrant scarring.

Delayed wound healing also can result in hypertrophic and keloidal scarring, and should be avoided when possible. Once the wound has closed, avoiding tension and stretching of the wound is beneficial. Commonly used techniques include fixable materials such as tape, bandages, and tight garments. Silicone gel sheeting and taping are helpful to avoid subjecting the wound to friction and tension during the healing process.6,7

**What are Additional Treatment Options for Keloid Scars?**

Current studies on the treatment of keloids are limited by the overall low quality of research, inconsistent measures of improvement, differing methodologies, challenges in differentiating keloids from hypertrophic scars, variable responses to treatment, and variable recurrence rates.12 In addition, the chronic and recurrent nature of this condition makes it difficult to assess recurrence and ensure adequate follow-up. Based on a review of the literature, intrallesional steroids, silicone gel sheeting, pulsed dye laser, and postexcision radiotherapy are promising areas of keloid treatment.12

**Corticosteroid injections**

Intrallesional corticosteroids are a first-line treatment for keloids and a second-line treatment for hypertrophic scars after other therapies have failed.13 They decrease the production of inflammatory cytokines and inhibit collagen synthesis and fibroblast proliferation. Reported response rates range between 50% and 100%, with recurrence rates of 9%–50%.8 Corticosteroid treatments soften and flatten scars, but they do not narrow or eliminate them.6

The recommended dosage is 10 mg/linear centimeters of keloid of triamcinolone acetate (10 mg/mL) every 2–6 weeks.8 Side effects of corticosteroid injections include severe pain during injection, hypopigmentation, skin and subcutaneous fat atrophy, systemic side effects (adrenal suppression), steroid acne, and telangectasias.

Corticosteroid monotherapy is associated with a high recurrence rate and may be more effective when combined with surgery.13 Corticosteroids after surgery are associated with a less than 50% recurrence rate.5 Surgical excision may be followed with intraoperative injection of triamcinolone acetonide, then weekly injections for 2–5 weeks and monthly injections for 4–6 months. Response without recurrence occurred in 91.9% of keloids and 95.24% of hypertrophic scars.13

Level 4 evidence supports positive results in combination with cryosurgery, pressure therapy, pulsed dye laser, pulsed dye laser with 5-Fluorouracil, and carbon dioxide laser with pressure therapy.12 A single case series study demonstrated negative level 4 evidence for corticosteroid injections.12

**Complete surgical resection**

Surgical resection of keloids has a high recurrence rate (between 45% and 100%) when used alone.6–8 Surgery removes bulk of the scar and reduces the width of the lesion, and mass reduction of the scar may result in improved symptoms. However, total excision may stimulate additional collagen synthesis with quick recurrence and possibly larger size.5,11 Intramarginal excision may be used to avoid stimulation of additional collagen synthesis.6

**Radiation**

Radiation therapy counteracts abnormal activated fibroblasts and promotes normal fibroblasts, thus
restoring the balance between collagen synthesis and breakdown. The best results are seen with 10–15 Gy over the course of 5–6 sessions. Irradiation is typically begun 24–48 hours after surgical excision of the keloid. The most frequent treatment studied was 900 cGy in fractions within 10 days of surgery. The sooner radiation is administered after surgery, the more effective it is at preventing recurrence. Radiation after surgery prevents recurrence in 75% of cases at 1 year, and adjunctive radiation after surgery results in efficacy rates of 65%–99% compared with excision alone.

Two studies provide level 2 evidence supporting postexcisional radiotherapy, with multiple supporting studies providing level 4 evidence. However, there is currently no consensus on optimal dose, timing, or schedule. Radiation monotherapy is controversial, with reported response rates of 10%–94% and recurrence rates of 50%–100%. Side effects include hyperpigmentation, ulcers, and risk of inducing malignant tumors; hence, radiotherapy is generally contraindicated in children, pregnant women, and areas of high carcinogenic potential such as the breast and thyroid.

Silicone gel sheeting
Silicone gel sheeting works by hydration and occlusion of the wound. It also results in a decrease in capillary activity, reduced collagen deposition, and temperature-mediated activation of collagen breakdown. Silicone sheeting also may alter growth factor secretion and influence fibroblast regulation.

Recommendations are to begin when an itchy red streak forms in the wound, with treatment for 12–24 hours daily for a minimum of 2 months. We recommend that patients tape the silicone gel sheet over the wound at night and leave it in place as long as possible. Problems associated with this therapy include moisture accumulation that can lead to skin maceration, persistent pruritis, skin rashes, odors, and poor patient compliance.

Although this is a well-accepted treatment modality, the studies to date provide level 4 evidence, with a lack of controls and increased susceptibility to bias. A recent Cochrane systematic review on the use of silicone gel sheeting for preventing and treating hypertrophic and keloid scars found that any effects were obscured by the poor quality of research.

Compression therapy
Compression therapy reduces collagen synthesis by limiting the supply of blood, oxygen, and nutrients to scar tissue. The resulting hypoxia leads to fibroblast and collagen degradation that encourages realignment of collagen bundles, hastens scar maturation, and relieves pruritus and pain. It is most effective when it is initiated immediately after reepithelialization of the wound and pressure is maintained between 24 and 30 mm Hg for 6–8 months, based on empirical evidence. Devices should be worn for 8–24 hours per day during the first 6 months of scar healing. This therapy is commonly used for hypertrophic burn scars, and patient compliance can be problematic. Additionally, pressures greater than 40 mm Hg can cause skin maceration and paresthesias.

Laser
Laser treatment of keloid scars is thought to result in thermal tissue reaction and selective photothermolysis. The light energy is absorbed by hemoglobin, resulting in heat and coagulation necrosis; it also may alter signaling pathways that favor collagen degradation and fibroblast apoptosis. Tissue-specific effects depend on the laser wavelength, and it has been shown that the pulsed dye laser resulted in substantial clinical and histologic improvement of existing keloids. The short-pulsed dye laser (585 nm) is effective at reducing symptoms, color, and height in keloidal scars. The newer long-pulsed dye laser (595 nm) also improves scar texture, color, height, and pliability, while decreasing scar erythema and symptoms. The carbon dioxide and Nd:YAG lasers are ineffective and are associated with high recurrence rates. There are some recent reports that nonablative fractional lasers may be helpful in the treatment of keloid scars; however, they are not widely used for this purpose currently. Most hypertrophic scars require two treatments to achieve 50%–80% improvement, and keloids typically require additional treatments.
Cryotherapy
Cryotherapy results in ischemic damage, which causes necrosis and reduction in the size of the tumor. Level 4 evidence supports its use, with 51–74% of patients experiencing keloid flattening. Cryotherapy works best on smaller newer lesions, and it also works better when combined with steroid injections. Side effects include pain, hypopigmentation, edema, infections, hypoesthesia, milia formation, and necrosis. This therapy is not as good a choice for individuals with darker skin because of risk of hypopigmentation.

Antitumor and immunosuppressive agents
5-Fluorouracil is a pyrimidine analog with antimetabolite activity, which inhibits DNA synthesis and targets rapidly proliferating fibroblasts. Level 2 evidence supports intralesional 5-Fluorouracil after surgery, with a reported recurrence rate of 19% at 1 year follow-up. Level 4 evidence also supports its use as monotherapy and as combination therapy with laser and steroids. Complications with this treatment include wound ulceration and hyperpigmentation.

Bleomycin blocks the cell cycle at G2, cleaves DNA, and degrades cellular RNA, resulting in necrosis of keratinocytes. Bleomycin 0.1% intralesional injections using the multiple puncture method every 3–4 weeks has resulted in flattening of keloids and relief of pruritis and pain. Dose-limiting side effects include pulmonary toxicity and hepatotoxicity, in addition to cutaneous side effects of hyperpigmentation, Raynaud phenomenon, gangrene, fibrosis, and alopecia.

Interferon-γ decreases collagen production and increases collagen breakdown by collagenase. It has potential efficacy as an antifibrotic therapy, but there are conflicting data on its efficacy in treating keloids. Level 4 evidence supports interferon-γ monotherapy and interferon-α2b combined with carbon dioxide laser. Currently, there is a lack of evidence on the long-term effectiveness of interferon-alpha or interferon-gamma as monotherapy or combination therapy.

Mitomycin C is an antineoplastic agent that inhibits DNA synthesis by cross-linking DNA. Limited studies demonstrate flattening and increased patient satisfaction when used to treat keloids. However, current studies offer no comparisons with standard therapies, and there is no consensus on the optimum dose, timing, or duration and frequency of treatment. Side effects include hyperpigmentation and skin atrophy.

Imiquimod is a topical immunomodulator that induces interferon-α and prevents fibrosis. Limited studies have been conducted on its use as postexcisional treatment of keloids. Level 4 evidence supports its use as postexcisional therapy based on a nonrandomized trial with four patients and a case series.

What is the Best Treatment for Keloid Scars?
There is no best treatment for keloid scars aside from prevention. Excision of keloids without further treatment clearly has an unacceptably high rate of recurrence. Whether the operative site is injected with steroids at the time of resection or treated with radiation therapy, treatment is individualized for each patient and the decision is made with consultation of a radiation oncologist.

We recommend treatment of small keloids with injection of steroids and application of silicone sheeting when possible. Patients are instructed to massage the scar daily and return for evaluation of the response to therapy in 6 to 8 weeks.

For larger keloids, those that must be removed for functional reasons, or keloids that do not respond to other therapies, surgical resection is scheduled after the patient has been evaluated by a radiation oncologist. If the patient is an acceptable candidate for postoperative radiation therapy, then this is arranged no more than 48 hours after surgical resection. If the patient is not a candidate for radiation therapy, then the surgical wound is injected with steroids after the patient has been counseled on the risks of atrophy and hypopigmentation of the skin as a result of steroid use.

During surgical resection of keloid scars, meticulous surgical technique is used, including minimizing electrocautery use and limiting the amount of suture material left in the wound. We recommend approximating the dermis with absorbable monofilament suture and closing the skin with subcuticular permanent monofilament sutures placed in such a fashion that they can be removed postoperatively.

When Should Patients Be Referred to a Plastic Surgeon?
Referral of patients should be based on individual practice patterns. Any physician who is interested in treatment of keloid scars and is educated on the currently accepted therapies should feel confident in treating these patients. If keloid scars are rare in an individual’s practice, then consideration should be given to referring the patient to a general surgeon or plastic surgeon with more experience in the treatment of these patients.
REFERENCES

In The Trenches
Practical Case Series

The Green Journal welcomes submissions of cases for the “In the Trenches” series. Cases (400 word maximum) considered by the Editors to illustrate clinical issues that are especially prevalent, challenging in women, and of high educational value will be chosen for potential publication. Case authors will work with the series editor to identify commentators. For more detailed information about “In the Trenches” requirements for authors, please visit http://edmgr.ovid.com/ong/accounts/inthetrenches.pdf. For questions, please contact Ingrid Nygaard, Clinical Case Series Editor, at ingrid.nygaard@hsc.utah.edu.

Let Us Hear From You

356 Lutgendorf et al Management of Keloid Scars

OBSTETRICS & GYNECOLOGY