Key Words: hypertrophic scar, keloid, wound healing, skin incision, Langer’s lines, treatment options

Abstract

Keloid and hypertrophic scars are due to increased fibroblastic activity within a scar. A keloid extends beyond the boundaries of the original injury, whereas a hypertrophic scar is kept within the boundaries of the original injury. Treatment is usually with intralesional steroids injected into the scar itself and repeated if necessary. Surgical excision of most keloids is unsatisfactory and quick recurrence occurs in 65-100% of cases unless adjuvant intralesional steroid treatment or radiotherapy is given. Surgical excision of a realigned scar in the direction of the natural skin crease with primary subcuticular closure has however a minimal recurrence rate. Central debulking has a lower recurrence rate than surgical excision especially for certain keloid scars. The previous gold standard treatment of surgical excision followed by radiotherapy is now less popular because of the risks of radiation. Innovations with adjuvant intralesional drugs post surgical excision are promising.

Introduction

Both hypertrophic and keloid scars are a result of an abnormality of healing caused by excess collagen formation. In a hypertrophic scar the hypertrophy stays within the limits of the original injury, but in a keloid scar the thickening extends beyond the scar, projecting above the level of the surrounding skin but rarely extends into underlying subcutaneous tissue. It tends to widen with time. Hypertrophic scars enlarge over about three months but then become softer and regress slowly although not necessarily completely. Keloids continue to enlarge for six months to a year and may never regress. Some keloids appear to arise spontaneously and present as multiple lesions as do keloids as a consequence of acne or chicken pox. Only humans are affected by keloids. They occur in all age groups but are rare in newborns or the elderly. The highest incidence is in those aged between ten and twenty. It is higher in young females than in young males, reflecting the greater frequency of ear-lobe piercing among females. Hypertrophic and keloid scars are both unsightly and uncomfortable (painful and pruritic) to the patient. They cause significant disfigurement if located on the face, contractures if overlying a joint and local bacterial infection can follow trauma-induced erosion. They are thus primarily of cosmetic concern. The most important risk factor is delayed wound healing due to prolonged inflammation from whatever cause e.g. foreign body, infection, burn, inadequate wound closure, or in areas of chronic inflammation.

Prevention is the first rule. Non-essential cosmetic surgery in patients known to form keloids should be avoided although the risk is lower among patients who have only ear lobe lesions. The risk of keloid and hypertrophic scars may be reduced by a) avoiding operating in sites where keloids commonly form - the upper back, upper central chest, breasts, shoulders and upper arms, b) avoid operating unnecessarily in patients who are at highest risk - the young and Afro-Caribbean patients, c) planning correctly and making the incision parallel to the skin tension lines, d) reducing tension on the wound by undermining and using subcutaneous sutures to increase wound strength.

Wound healing

There are competing influences in wound healing. The laying down of fibrous tissue and the digestion of this tissue to modify the shape of the scar are normally in balance. If little fibrous tissue is laid down or it is digested excessively,
then dehiscence is likely. This can be predicted in patients who have undergone radiotherapy at the wound site, in patients on steroid medication and in patients with Ehlers-Danlos syndrome or diabetes. In other circumstances, deposition of fibrous tissues is excessive and results in a heaped-up, hypertrophic or keloid scar.²

**The balance of forces in wound healing**

| Collagen synthesis | Wound Dehiscence | Scar | Collagen breakdown |

Most scars pass through a stage in which they are red (due to increased blood supply) and hard (due to excess collagen and fibrous tissue). After several months, spontaneous maturation usually results in a pale soft scar. During the period of scar maturation, collagen synthesis often exceed collagen breakdown; and reoperation to attempt to improve the appearance of the scar at this stage is extremely unwise. Scar revision for adverse scarring should be delayed for at least 18 months as resolution to mature scar occurs over a period of 12-18 months.¹²

Kischer and Brody³ declared the collagen nodule to be the identifying structural unit of hypertrophic scars and keloids. The nodule is absent from mature scars, contains a high density of fibroblasts and unidirectional collagen fibrils in a highly organized and distinct orientation. Keloid and hypertrophic scars differ from healthy skin by a rich vasculature, high mesenchymal cell density, and thickened epidermal cell layer. Attempts to differentiate keloids from hypertrophic scars clinically have proved difficult in the early phases of formation. Clinical differences become more apparent as lesions mature. The most consistent histological difference is the presence of broad, dull, dense eosinophilic (pink) whorls and bundles of collagen with an overlying thin epithelium without normal skin appendages.⁴

A keloid scar is normally easy to recognize but it is important not to confuse a rather round, protuberant keloid scar with a cyst, since biopsy of such lesions can exacerbate the problem of scarring. Dermatofibrosarcoma protubersans and lobomycosis may also mimic a keloid scar.¹

**Risk Factors**

The exact mechanisms of the pathogenesis of keloid and hypertrophic scars continue to be an enigma but the risk factors are similar for both hypertrophic and keloid scars.

**Genetic basis:** The increased prevalence paralleling increased cutaneous pigmentation suggests a genetic basis or at least a genetic linkage - a genetic predisposition which is more likely with pigmented skin. They are most commonly found in patients of African origin but can be found in all races - 16% of a random sample of black Africans had keloids. Polynesians and Chinese are more prone to keloids than Indians and Asians whereas white people are least commonly affected. They are associated genetically with HLA-B14, HLA-B21, HLA-Bw16, HLA-Bw35, HLA-DR5, HLA-DQw3, and blood group A. The tendency may run in families as they have both dominant and recessive modes of inheritance.⁵,⁸

**Tension on the wound.** When an elective incision is to be made, it is always wise to place the scar in an established skin crease or along a line of little tension (Langer’s lines).⁶ These contours, along which more favourable scarring occurs are called Langer’s lines. On the cheek an oblique scar which runs along the nasolabial crease or parallel to it will often heal extremely well whereas a transverse scar, such as that inflicted in knife fights, usually stretches and becomes red and hypertrophic. If wrinkling has not developed its likely pattern on the face can be found by asking the patient to smile and to frown, and on the extremities by flexing and...
extending them. On the completely smooth skin of a child it can be extremely difficult to select the best line or position for a scar, especially at sites distant from the eyes and the mouth. On the ear, the contour lines of the pinna are useful in guiding scar placement. A natural junction like that between the nose and face around the base of the alae may be useful to hide a scar. A subcutaneous lipoma of the forehead may be approached through a scar in the hairline, for example, and a lipoma in the cheek area through a small incision hidden in a pretragal site. With the advent of endoscopic surgery it is often possible to remove lesions through a remote access port.

**Delayed healing:** This usually occurs as a result of wound infection or if wound edges are not apposed. This will lead to healing by second intention as the defect fills gradually with granulation tissue and restoration of epidermal continuity may take a considerable time. Healing by second intention usually results in prolonged healing, excessive fibrosis and an ugly puckered scar as opposed to healing by first intention which occurs following the meticulous apposition of the edges of clean incised skin. This leaves a narrow epidermal defect which can be bridged easily resulting in a fine hairline scar. Thus healing by second intention is more likely to develop keloids especially if healing time is greater than three weeks. It may be possible to compromise delayed healing by freshening the wound edges and bringing them into apposition or by covering the defect with a skin graft.

The timing of suture removal is crucial, and depends on various factors, especially the site. Untimely removal may predispose healing by second intention and risk keloid formation. Late removal may predispose prolonged inflammation from the sutures (foreign body) leading to delayed healing, unnecessary marks on the skin and may encourage infection. The loose sutures used to close the upper or lower eyelid wounds of a blephoroplasty are often removed at 48h. Elsewhere on the face, sutures are removed at between four and five days. Where movement increases the risk of dehiscence - in hand and limb wounds for example - it is common to leave sutures for ten days. The use of absorbable sutures certainly avoids the need for suture removal and may be helpful in children, but it should be noted that sometimes the quality of the scar may be impaired by the process which dissolves the sutures.

**The site of the scar:** Scars over the sternum and deltoid areas are particularly prone to becoming hypertropic or keloid. The presternal zone, the ear lobes and the deltoid areas are common sites for keloid scarring. Scars over joints or the axilla can cause contractures. A Z-plasty is useful in relieving the contracture. A Z-plasty may reduce hypertrophy of a scar but not keloid formation.

![Herpes zoster keloid scar in HIV patient](image1)

![BCG keloid scar in high tension area (shoulder)](image2)
Treatment Options

Keloids rarely resolve spontaneously but with treatment they may become softer, less tender, painful and pruritic. Treatment of hypertrophic or keloid scarring can be difficult and the results are not easy to predict because there are many factors involved. Preoperative evaluation is critical to assess a patient’s motivation for treatment and to assess the ability to participate in long term care and follow-up. Treatment options include intralesional steroid injections, compression, silastic gel therapy, excision and re-suturing, excision and adjuvant intralesional steroid therapy or radiotherapy, central debulking and carbon dioxide lasers.\(^1\,8,17\)

Intralesional Injections

Repeated injections into the main body of a scar with long lasting steroids such as triamcinolone (10mg/ml) may soften and shrink it.\(^10\) Initially the injections are difficult to administer because the scar is very dense. With time, however, it softens and the treatment is easier to give. Corticosteroids reduce excessive scarring by reducing collagen synthesis (juvenile collagen), altering glucosaminoglycan synthesis, and reducing production of inflammatory mediators and fibroblast proliferation during wound healing. It is helpful in treating both developing and established keloid scars. Triamcinolone reduces the size of most keloids but does not eliminate them. This may however be the best treatment in some cases as a single modality or as an adjunct to excision. We use them post excision of keloids for the early-developing itchy scars and repeat if necessary after six to eight weeks. Some scars will respond readily to one or two injections, in others even a prolonged series of injections are not helpful. As a single modality, response rates varied from 50-100% with recurrence rates of 9-50% in completely resolved scars. As an adjunct, postoperative intralesional injection yielded a recurrence rate of 0-100%; most studies citing a rate of <50%. Injections of hypertrophic scars are similarly repeated at monthly intervals for three to six months or longer if necessary until the scar is soft. Excessive injections and injecting into the surrounding skin are avoided as this may cause skin atrophy, telangiectasia and pigmentary alteration. Systemic treatment is valueless.\(^1,10,1\)

Excision

Excision and re-suture may not prevent keloid formation. Excision of keloids, like excision of hypertrophic scars, only temporarily cures the problem. It has been shown to yield 65-100% recurrence rate. A larger lesion will develop in its place and this treatment is to be condemned unless followed by adjuvant triamiconolone intralesional injections or radiotherapy.\(^1,10,14\) Excision surgery in combination with adjunct measures can be curative. However, healing can occur by first intention without adjuncts in a low tension site if a scar transgressing Langer’s lines (natural skin creases), is converted into a natural skin crease scar by means of a larger elliptical excision with its longitudinal axis parallel to the lines of skin tension.\(^1,7\) This is followed by a tension-free primary subcuticular closure using preferably fine absorbable suture (e.g.monocril). Subcuticular sutures approximate the skin edges without leaving cross-hatching or suture marks. Adjuvant intralesional steroid therapy is given only if necessary i.e. evidence of recurrence. Simple excisional surgery should involve the least amount of soft tissue handling to minimize trauma, and closure planned with minimal skin tension along relaxed skin tension lines. All attempts should be made to remove any source of postoperative inflammation, such as trapped hair follicles, foreign material, hematomas or infectious areas. In an attempt to reduce wound tension, both full and split thickness skin grafts have been used, but these have only been partially successful.\(^1,7\)
Excision and radiotherapy

In patients who do not respond to the methods outlined above, keloid scars may be excised and treated subsequently (at most 24hrs later) with radiotherapy to suppress fibroblast activity and minimize the risk of recurrence. This treatment, although the gold standard for keloid scars at present, is not universally successful and cannot be repeated. X-irradiation has been shown to have some effect in a small dose (the ‘antikeloid skin dose’), but to use radiotherapy in non-malignant disease runs counter to all modern thinking. Recurrence is not uncommon, and this technique is unsuitable for young patients as late side effects of radiotherapy may develop. When excisional surgery is followed by postoperative radiation treatment, the total fractionated dose should be a minimum of 12Gy, according to a comparative study showing a higher recurrence rate for patients treated with total doses less than 12Gy.1,1

Central debulking

Central debulking of keloid is useful for scars running on natural skin creases (Langer’s lines) but with minimal free adjacent skin that could be undermined and raised for a non-tension primary closure e.g. nuchal and ear lobe keloids.1 Our recent and short experience of excising the central bulk of the keloid tissue, keeping the margin of excision at the lateral borders and in depth within the keloid tissue, preserving a rim of keloid tissue at all margins and closing the wound primarily by keeping all sutures within this rim have shown minimal recurrence as compared to complete excision. The reason might be because the definitive causative collagen nodules have simply been ‘cored-out’ from its surrounding capsule with minimal trauma to surrounding skin. Secondly. because these keloid scars are on natural skin creases with minimal tension, central debulking may not trigger the excessive collagen regenerating activity of fibroblasts. There may be a decreased inflammatory or immune response to central debulking.

centrally debulked keloid

An alternative surgical management of massive nuchal keloids is to utilize the Radovan tissue expander in the scalp below the galea and immediately adjacent to and above the keloid. This may create adequate hair-bearing scalp which could be advanced to cover the defect when one resects the tumour mass. In the past the technique of resecting large keloids of the occipital, parietal and nuchal areas of the scalp and covering the defect with full-thickness grafts from the thigh met the problem of an aesthetic defect devoid of hair and not amenable to surgical hair replacement.1,7,10

Tissue expanders have also been used to create additional skin for repair of third-degree facial burns.7,12

Central debulking and excision

Figures 5, 6, 7

centrally debulked ear lobe component and excised facial component. Followed – up within 3 months.
(with permission)
Intralesional steroid can be administered postoperatively, or if there is evidence of recurrence. Further debulking can be done if there is redevelopment of keloid.\(^1\)

**Carbon dioxide lasers**

Although the use of carbon dioxide lasers to cut away keloid scars is thought by many authors to minimize the risk of keloid recurrence, success is not guaranteed. The recurrence rate approaches 90%. It may be that the use of lasers can delay rather than prevent recurrence, and in certain hopeless cases it would seem appropriate to recommend a technique of repeat excision. The advantage of laser therapy is that it is a precise hemostatic excision with minimal tissue trauma thereby minimising an excessive inflammatory reaction. Carbon dioxide laser ablation associated with interferon alfa 2b injections reduces the recurrence of keloids.\(^13\)

**Recent developments:**

Innovations with adjuvant intralesional drugs such as interferon(IFU), 5-fluorouracil(5-FU), doxorubicin, bleomycin, verapamil, retinoic acid, imiquinoid 5% cream, tracolimus, tamoxifen, botulinum toxin and over-the-counter treatments (onion extract, combination of hydrocortisone, silicone, vitamin E) used as a monotherapy or in combination with other drugs post surgical excision are promising.\(^1,14-17\) Ahmed (1998) has proposed the use of an enzyme from the papaya fruit to shrink or modify keloid scars.\(^18\)

It seems likely that enzymic digestion of excess collagen within unsightly scars might be possible in future. Other promising therapies are the antiangiogenic factors, including the vascular endothelial growth factor(VEGF) inhibitors (e.g.bevacizumab), phototherapy (photodynamic therapy - PDT), UVA-1 therapy, narrow band UVB therapy, transforming growth factor (TGF)-β3, tumour necrosis factor (TNF) alpha inhibitor (etanercept), and recombinant human interleukin (rhIL-10) which are directed at decreasing collagen synthesis.\(^14\) It is thought that the transforming growth factor molecule (TGFβ) is important in orchestrating excessive wound healing as scarring of animal embryos after intrauterine surgery is often minimal. When drugs designed to block the activity of this molecule are applied to healing wounds it may be possible to suppress scar hypertrophy.\(^16\)

Studies so far have been relatively small in scope and further investigations are needed in regard to safety, adverse effects and efficacy of these therapies.

**Follow-up**

Because of the high rate of recurrence a follow-up period of at least a year is necessary to evaluate fully the effectiveness of therapy. Non-compliant patients who are lost to follow–up care for months often return for evaluation long after further adjunct treatment would have been most beneficial.

**Conclusion**

Keloids and hypertrophic scars are benign dermal fibroproliferative tumours with no malignant potential. The two main factors known to favour the production of a cosmetically attractive scar are making the incision parallel with Langer’s lines thus minimizing tension, and avoiding wound infection. The best form of treatment of hypertrophic and keloid scars is avoidance, and this may be achieved by recognition of the potential for scarring. Of the many therapies listed, nothing is reliably definitive. This highlights the essential problem in keloids i.e. no clear molecular mechanisms is defined for keloid development. Increased understanding at the molecular level will lead to development of new therapies. Further basic scientific research is required on the prevention and treatment of hypertrophic and keloid scars.

The old saying ‘prevention is better than cure’ has never been more true.
References


