EAR KELOIDS: A REVIEW AND UPDATE OF TREATMENT OPTIONS

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Abstract.

Ear keloids are among the most challenging plastic surgery conditions and may have significant psychosocial impact for the patient. Their aesthetic considerations are serious and despite a variety of treatment options, they often proved to be recurrent. This paper reviews the management options of ear keloids available in literature up to date. Multiple therapeutic options are discussed, such as: surgical treatment, corticosteroid injections, laser therapy, cryotherapy, radiotherapy, pressure therapy, therapy with antitumor or immunosuppressive agents.

Keywords: Ear lobe, keloid, monotherapy, combined therapy.

The natural response of the body to a traumatized tissue is the scar. The wound healing process has three different phases: the first is the inflammatory phase, the second - the proliferative phase or the granulation phase and the third is the remodeling phase or the maturation phase [1]. When there is an imbalance between anabolic and catabolic phases of the scar formation, the result is the appearance of a pathologic scar. Two types of excessive scars are described: hypertrophic scar and keloid, as a result of an aberrant healing process. The difference between the two entities is a hot topic in the medical literature. Clinical, histopathologhical, immunohistochemical and electron microscopic differences have been described [2].

Epidemiology. The keloid scar was observed to occur in individuals of all races, but more frequently in the darkly pigmented individuals, with an incidence of 6% to 16% in African populations [3,4]. The keloid appearance is about 15 times greater in dark skin individuals than in whites [5]. Higher incidence was observed during puberty and pregnancy, periods with hyperactivity of the pituitary gland [6].

The keloid scar has a genetic predisposition and an autosomal dominant inheritance pattern was demonstrated [7,8]. Familial keloids have been described in two rare syndromes: Rubinstein-Taybi syndrome (OMIM 180849) [9,10] (broad toes and thumbs, characteristic facies, mental retardation and increased frequency of keloid scars) and Goeminne Syndrome (OMIM 3134300) [10,11] (keloids, torticollis, renal dysplasia and cryptorchidism).

Clinical features. Unlike the hypertrophic scar which stays within the original scar boundary, even if it continues to rise, the keloid scar grows beyond the boundaries of the initial wound. Keloid scars appear as firm nodules and generally do not spontaneously regress. Frequently, the patients accuse pruritus and pain [12]. In Caucasian patients, the keloid scars are erythematous and telangiectatic, while in darker skinned patients they are hyperpigmented. The most affected areas are: chest, shoulders, upper back, back of the neck, cheeks and earlobes. It was believed that keloids appear most often in areas of high skin tension. In contrast to this idea, palms and soles are rarely affected by keloid, and the ear lobe, area with minimal skin tension, is one of the most common sites of keloids appearance [10]. Unlike hypertrophic scars, which, after reaching a certain size, stabilize or even regress, the keloids do not regress spontaneously and they may even continue to grow with time (Table I).

Pathogenesis. The keloid formation process is poorly understood. It is known that it appears in predisposed individuals in presence of a trigger, such as skin trauma. The skin trauma might be secondary to surgical wounds, burns, body piercings, folliculitis, acne. Most of the keloids develop in the first 3 months, but some may appear up to 1 year after skin trauma [12].

Recent studies show that both the severity of inflammation and the type of immune response predispose to

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the formation of excess scar tissue. In the scar, densely populated by inflammatory cells, fibrogenic factors like transforming growth factor (TGF)-β1 and β2 are released. The decreased levels of TGF-β3 and matrix metalloproteinases [MMP] lead to accumulation of extracellular matrix (ECM). Development of a Th-2 response stimulates fibrogenesis and Th-1 predominance attenuates the tissue fibrosis. The scar tissue of keloids presents a more prolonged inflammatory period. All these may help to explain why keloid scars spread beyond the margins of the original wound [13].

Ear keloids treatment options

Although there a lot of information about histomorphological structure of keloids in current literature, there is no guideline regarding the treatment. There are various treatment methods described, such as surgical excision, intralesional injection of corticosteroids, compressive therapy, radiotherapy, laser therapy, cryosurgery, therapy with antitumor or immunosuppressive agents and combinations of these methods. The reported success rate is variable. This is why most doctors combine treatment modalities.

Surgical treatment

Surgical excision alone leads to a high recurrence rate, between 50-100% [14,15]. Therefore it is rarely used as monotherapy.

Surgical removal of excessive scar tissue returns the wound to the initial state and further postoperative scaring can be reduced by adjunctive therapies [14] (intralesional corticosteroid injections, radiotherapy, pressure therapy, immunomodulators). A retrospective cohort study on 2002 patients found multimodal therapy (excision followed by combination of steroid and radiation therapy or steroid and silicone gel therapy) entailing less recurrence than post-excisional steroid alone [15].

Excision can also be used for large keloids, for debulking or removal of infected regions [16].

There are case reports about the usage of dermal substitutes after keloid excision followed by brachytherapy or imiquimod cream with encouraging results [17,18,19]. Also, core excision (with low-tension wound closure) or shave excision of earlobe keloids associated with steroid injections, postoperative pressure device application, imiquimod 5% cream, or cryotherapy on surgical scar provided a good esthetic result [20].

Intralesional corticosteroid injections

Effects of corticosteroids are due primarily to their suppressive effects on the wound inflammation [21] and secondarily to the reduction of collagen and glycosaminoglycan synthesis, inhibition of fibroblast

Table I. Differences between hypertrophic and keloid scars.

	Hypertrophic scar	Keloid scar
Clinical appearance	• Develops soon • Stays within the original scar boundary • Improves with time • Tends to flatten with time • Appears when scars cross joint, skin creases at a right angle • No association with skin color	• May appear after months • Grows beyond the boundaries of the initial wound • Rarely improves, usually develops with time • Raised, firm, pruritic, painful • Do not spontaneously regress • Occurs on the ear lobe, sternal notch, shoulders, upper back, back of the neck, cheeks • Associated with dark skin
Histopathologhical	• Collagen fibers oriented parallel to the long axis of the epidermal surface • Nodules of high density fibroblasts and collagen in the middle or deeper scar's layer • Small blood vessels oriented vertically around the nodules • 20-30% mast cells in reticular dermis	• "Keloid collagen" (thick and hyalinized collagen) arranged in a hazard pattern • Absence of nodules • Small blood vessels under the epidermis appearing to grow out in the scar • 73% mast cells in reticular dermis
Immunohistochemical	• No α-SMA expressing myofibroblasts	• α-SMA expressing myofibroblasts present in a third of cases • Higher $CD_4(+):CD_8(+)$ ratio
Electron microscopic		• The collagen fibers separated from the fibroblast's membrane by a amorphous substance

growth [22], as well as enhanced collagen and fibroblast degeneration [23]. They can be used as first line therapy, with good response rates from 50 to 100% and recurrence rates between 9% and 50% [24]. Side effects which include hypo- or hyperpigmentation, telangiectasia, skin atrophy and pain upon injection can be encountered in up to 63% of patients [25]. The latter can be reduced by using EMLA or the addition of lidocaine. A range of steroids can be employed, the one used most frequently is Triamcinolone acetonide at a concentration of 40 mg/mL, administered by intralesional injections, at monthly intervals for up to 6 months [26]. When used in conjunction with surgery, local steroid therapy is initiated before surgery and continued postoperatively, monthly, for at least 3 months [25,27]. Rosen et al [28] treated ear keloids with excision and intraoperative and postoperative injection of steroids and reported a recurrence rate of 23%. Shons et al [29] evaluated 31 earlobe keloids in 20 patients. After surgical excision of the scar and adjunctive therapy using three postoperative injections of triamcinolone; in a follow-up period of 12 to 62 months, only one keloid recurred.

Corticosteroid injection in association with 5-fluorouracil, pulsed dye laser, and cryotherapy has been reported to be more efficient than corticosteroid alone, although there are few randomized controlled studies [30,31,32].

Cryotherapy

The freeze induces vascular damage that may lead to anoxia and ultimately tissue necrosis [33]. Common side effects include permanent hypo- and hyperpigmentation, blistering, and postoperative pain [34], and a delay of approximately 3–4 weeks between sessions (approximately three to six sessions are needed) is often needed for post treatment healing [35,36]. Cryotherapy produces substantial flattening of the keloid scars [37], one study reported improvement of the scars aspect in 73% of the patients. No recurrence cases were reported [33]. Another study also presented good results using cryotherapy alone for ear keloids in young patients [38].

Laser therapy

Various laser types have been used for keloid treatment: CO2, argon, Nd:YAG and PDL lasers with mixed results. Argon and Carbon Dioxide lasers have not been shown to be highly effective [39,40]. A review by Bouzari et al established that the optimal wave length is currently the 585 nm PDL, although the recent results of the Q-switched, 532 nm, frequency-doubled Nd:YAG laser are promising [41].

Radiotherapy

Surgery with postoperative radiation therapy has been suggested to more effectively treat keloids than radiation monotherapy [42] with a success rate of 67 to 98% [43,44] and a recurrence rate under 10% [45,46].

The radiation was delivered as external-beam radiotherapy with superficial X-rays, Sr-90 brachytherapy or electrons and low-dose-rate brachytherapy [47,48,49]. Guix et al [50] found that high dose-rate brachytherapy is more effective than superficial x-ray or low energy electron beam administration. A review by Ogawa et al suggested that for maximal efficacy and safety, postoperative radiation therapy for keloids in adults should involve the application of 10 to 20 Gy delivered as 5 Gy per fraction [51]. In the same study they concluded that the risk of carcinogenesis from keloid radiation therapy was very low when adequate doses were used and adequate protection was provided for the surrounding tissues (including the thyroid and mammary glands) especially in children and infants. For the ear lobe, a protocol with 10 Gy in two fractions over 2 days is the dose suggested by Ogawa in another study [52].

Silicone gel sheeting

A meta study of 27 trials proved that silicone gel sheets are effective for management of keloid scars [53]; also they are useful in preventing the recurrence of hypertrophic scars and keloids in 70% to 80% of cases [54].

They should be applied after reepitheliaization and worn for at least 12 h a day for several months. The mechanism of action is unclear but through maintenance of wound hydration they improve scar quality [55].

Pressure therapy

The ear is easily amenable to pressure therapy. It is used as an adjunct post-excision therapy. The mechanism of action is unclear, but it is thought that pressure-induced localized hypoxia results in fibroblast death [56]. Various devices have been conceived to apply pressure therapy on the ear from magnets [57] to methyl methacrylate stents [58].

Therapy with antitumor or immunosuppressive agents

5-Fluorouracil (5-FU) inhibits the proliferation of fibroblasts. At the beginning, most studies used the high-dose version of 5-FU therapy (40–50 mg/mL). Starting with 2006 a "low-dose" therapy using 1.4–3.5 mg/mL 5-FU was promoted [13]. Bleomycin sulfate is thought to inhibit collagen synthesis, due to decreased stimulation by TGF-β1. Monotherapy with intralesional 5-FU [59] or bleomycin tattooing [60,61] produced scar flattening in 88% and 92% of treated patients, respectively, and no recurrences in the initial responders.

Mitomycin C, through a mechanism of DNA synthesis inhibition, inhibits fibroblast proliferation, protein and collagen synthesis, and angio-neogenesis. In a study on 26 pinna keloids, in 20 patients, Gupta and Narang used combined therapy of shaving surgery and mitomycin C solution of 1 mg/ml applied locally with a contact time of 3 minutes, right after the surgery and 3 weeks later. The patients were followed-up between 6 and 24 months and no recurrences were noted in this period [62].

Other innovative therapies, such as imiquimod 5% cream, photodynamic therapy, or botulinum toxin. A may also be important, but the information available up to date is contradictory and makes it less possible to define certain recommendations.

Conclusions. The aesthetic considerations of ear

keloid are serious, especially in young patients. Numerous management strategies have been proposed for ear keloid treatment but none of these is ideal. Better results are obtained using various combinations of the therapies mentioned above than in monotherapy. Although, articles dealing with ear keloid treatment are well represented in the medical literature, most of them are on a small number of cases and the follow-up period is reduced.

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