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Research Article

Ear Keloids Treatment, Update and our Protocol, Clinical Experience

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Abstract

The ear is a frequent target of keloid scars, one of the most difficult pathologies to treat with a high percentage of recurrence and generates a great challenge for physicians. Keloids of the ear are common in young population, especially females, causing serious aesthetic and psychological sequalae.

Despite the multiple treatments described in the literature to manage ear keloids, there is no consensus on treatment with scientific evidence that provides an efficacy that exceeds 80%.

We present the treatment protocol of the Plastic Surgery Department, Hospital Privado Rosario, Argentina, for ear keloids in the last 5 years with combined therapy in 18 patients and 23 ears (5 bilateral cases). This protocol consists in 4 stages: 1st. stage: surgical resection of the keloid mass, 2nd. radiotherapy stage (high dose rate brachytherapy) within the first 6 hours post-resection, 3rd. pressotherapy stage between 24-30 mmHg with thermo-malleable acrylic sheet, application of gel and silicone sheet and finally the 4th. stage at 4 weeks with intralesional infiltration with triamcinolone + 5-fluorouracil.

Keywords: plastic surgery; surgical technique; microthrombosis

Introduction

The keloid scar is the result of an abnormal regenerative response to skin injury. It is characterized by presenting elevated skin, firm, rubbery, fibrous nodules, colour changes, and by extending beyond the limits of the initial lesion. Keloids can be itchy or painful. They may also grow to be quite large and may distort or deform the ear. This last property distinguishes it from hypertrophic scars, another form of exacerbated growth of scar tissue [1].

The affected areas by anatomical topography are thorax (34%), shoulders (17%), upper extremities (13%), lower extremities (10%), and the ear (9%). In this last region, it occurs more frequently on the lobe, showing mainly spheroidal and reniform morphology, the latter being the most common [2].

The first description is attributed to the Egyptians and appears in the Edwin Smith papyri [3]. In 1806, Alibert coined the term keloid from the Greek term "crab claw". Cosman documented the characteristics and treatment of keloids in the first systematic review on the subject in 1961. Subsequently, Al-Attar and Mustoe defined the clinical differences between keloids and hypertrophic scars [4-5].

Among the hypotheses to explain the formation and growth of keloids are:

1. Increased growth factor activity (transforming growth factor beta and platelet-derived growth factor).

2. Alteration in the extracellular matrix (increase in fibronectin, aberrant production of proteoglycans and decrease in hyaluronic acid levels).

3. Abnormal regulation of the collagen balance (thicker, abnormal collagen fibbers and existence of nodules). Both, steroid-infiltrated and radiated keloid scars, show a decrease in collagenase inhibitors and an increase in fibroblast apoptosis, leading to a normalization of collagen network levels.

4. Mechanical stress. Mechanical stress on a scar misaligns the orientation of the collagen fibbers and causes a keloid scar. Abnormal scars rarely occur in older patients whose skin is no longer tense. However, the two most frequent sites for keloids are the thorax and the earlobe, whose tensile strengths are not similar. Force and tension are postulated to be important factors in the final appearance of scarring; however, it is possible that they

play a more important role in the pathogenesis of hypertrophic scars than in keloid formation.

5. Genetic immune dysfunction. Some studies suggest the association of blood group A, as well as human leukocyte antigens B14, BW35, DR5 and DQW3 in patients with keloids. Multiple reports point to alterations in serum complement and immunoglobulins G and M in patients with keloids. Clinical evidence suggests that patients who develop keloids have an inherent hypersensitivity of the cell-mediated immune system.

6. As an immunological reaction to sebum. Dermal injury exposes the pilosebaceous unit to the systemic circulation thus initiating a cell-mediated response in individuals who have sebum-sensitive T lymphocytes [4].

Multiple alternatives have been used to treat keloid scars, including surgical excision, radiation, cryotherapy, pressotherapy, the use of silicone gel sheets, lasers, and pharmacological agents such as corticosteroids, vitamin A, imiqui-mod, beta-aminopropionitrile or zinc oxide, which as monotherapy are not satisfactory in reducing symptoms or cosmetic improvement, since none achieves definitive control providing only partial improvement [6]. Treatment Aggressive surgical resection is often the only option for many patients, but excision alone carries unacceptably high recurrence rates of 45 to 100% [7].

Among all these options, surgical removal of the keloid associated with postoperative radiotherapy is considered the most effective treatment [8] since it presents higher success rates in the immediate postoperative period, with recurrences from 10 to 70% depending on the location. cause, type of patient and radiotherapy protocol used [7].

Postoperative radiotherapy is a procedure well accepted by patients and without serious side effects [8]. Its mechanism of action is based on the generation of microthrombosis and acute inflammation together with the control of proliferation and premature induction of cell death of fibroblasts [9] and the destruction of the basal cells of the dermis, thus producing a decrease in collagen synthesis [10]. Among the currently existing radiation techniques, those used for the treatment of keloids include electron beam radiotherapy and brachytherapy, with their different modalities [11].

Intralesional or topical corticosteroids are considered the standard treatment as they inhibit the transcription of nitric oxide synthetase (NOS) [12]. The NOS inhibits the synthesis of collagen by fibroblasts, the growth of keloid fibroblasts, the degeneration of these, and downregulation of type I collagen gene expression [12].

5-fluorouracil (5-FU: a pyrimidine analogue), is used mainly as a chemotherapeutic agent. Its mechanism of action in the formation of keloid scars has been suggested through the inhibition of fibroblast proliferation [13]. Results with intralesional application have been compared with pulsed light laser treatment and corticosteroid monotherapy; superior result in combination with the latter (88%) [14].

In this way, we proposed a protocol treatment for keloids of the ear in 4 stages. This protocol was developed in the Plastic Surgery Department at the Hospital Privado Rosario, Rosario, Argentina. As specific objectives we propose:

1st. Stage: 2nd Surgical resection of the keloid mass and intralesional infiltration at the end of the procedure (triamcinolone + 5-fluorouracil).

2nd. Stage: Radiotherapy stage (high dose rate brachytherapy) within the first 6 hours post-resection.

3rd. Stage: Pressotherapy between 24-30 mmHg with thermo-moldable acrylic sheet, application of silicone gel.

4th. Stage: Intralesional infiltration with triamcinolone + 5-fluorouracil.

Material and Method

We included 18 patients (10 men and 8 women) in our series of keloids of the ear at the Hospital Privado de Rosario, Argentina. We treated a total of 23 keloids (5 was bilateral lesions) that had received or not previous treatment in the period between 2018 and 2022. The institutionalized protocol for the treatment of keloids was carried out in all patients.

1st. Stage: Surgical technique

We begin with the resection of the keloid mass under local anaesthesia (2% xylocaine with epinephrine diluted in the same proportion with physiological solution, forming a 40 cc solution to which 500 mg tranexamic acid is added), previous asepsis and antisepsis with chlorhexidine soap solution. Surgical resection is performed with cold scalpel, haemostatic control is performed and we proceeded to primary closure or with a randomized local skin flap using suture in the subcutaneous cellular plane or deep dermis with material absorbable monocryl 5-0 and on skin with non-absorbable 5-0 monofilament nylon suture (FIGURES 1 AND 2). At the end of the procedure, 1 cc of a combination of 0.2 cc of triamcinolone and 0.8 cc of 5-fluorouracil is placed on the edges of the wound.

We send samples of the keloids for study by Pathology for research purposes.

The patient is discharged after 2 hours and is referred directly to radiotherapy at the Radiant Therapy Centre of the Gamma Group to start the 2nd. stage of the treatment protocol.

2nd. Stage: Radiotherapy

In our Radiotherapy Centre (Terapia Radiante Cumbres) the patient received high-dose brachytherapy-type radiotherapy using extradermal catheters that are placed in the radiotherapy session. Through it, the catheter is connected to the Selectrón brachytherapy equipment and, by means of a computerized system, it positions the radioactive source of Iridium-192 in the extension of interest immediately after the surgical intervention, within the following 6 hours. The treatment received was strictly confined to the region of the resected keloid. All patients received an approximate dose of 15 Gy in 3 fractions, administered on consecutive days (5 Gy per day), each session lasting 10 to 15 minutes. In all cases, a 5-mm (bolus) tissue-equivalent material gel was applied to the scar, to allow the skin surface to receive the full radiation dose and to limit the depth of electron penetration. To achieve adequate scar coverage, we use a 1 cm safety margin around the scar, protecting the surrounding skin from the margin with lead blocks.

In the follow-up after treatment, we recorded local symptoms and signs such as local erythema, pain, and pruritus.

3rd. Stage: Pressotherapy

The patients were controlled on day 4 post-surgical resection where pressotherapy with thermo-moldable acrylic sheet (Acuaplast®) is started, inducing an estimated pressure between 24 to 30 mmHg so that it is effective during the day (FIGURE 3). This pressotherapy is removed at night where a a silicone gel is used for the next 3 months.

The patients were controlled to remove the sutures between the following 7 and 14 days.

4th. Stage: Intralesional infiltration

After 21 days, intralesional infiltration was applied to each patient with a mixture of triamcinolone + 5-fluorouracil in a ratio of 0.2 cc and 0.8 cc respectively (FIGURE 4). This procedure was repeated every 21 days until completing 3 doses. During all this stage, the pressotherapy explained in stage 3 is continued for 3 months.

The recurrence or not of the keloids in all or part of the treatment area was evaluated, according to the definition of keloid recurrence proposed by Viani, et al. 2009 [15].

Discussion

Multiple alternatives have been used to treat keloid scars, including surgical excision, radiation, cryotherapy, pressotherapy, the use of silicone gel sheets, laser and pharmacological agents such as corticosteroids, vitamin A, imiquimod, beta-aminopropionitrile or zinc oxide, which as monotherapy are not satisfactory in reducing symptoms or cosmetic improvement, since none achieves definitive control, providing only partial improvement [6]. Treatment with aggressive surgical resection is often the only option for many patients, but excision alone carries unacceptably high recurrence rates of 45 to 100% [7].

For the treatment of mature keloids, therapy with intralesional corticosteroids, according to the recommendations of some consensus guidelines, became the first-line treatment with or without additional therapy. [16].

In our experience, the 4-stage treatment protocol for ear keloids was effective, with no recurrence in the 18 patients treated, including those who had received previous unsuccessful treatments with other modalities. The beneficial effect of combined therapy in the treatment of keloid scars is well known, managing to reduce recurrences by up to 10% [17]. (FIGURES 5-37].

To achieve this, we must respect each step of the protocol, beginning with the resection of the keloid mass and the closure technique of the surgical wound is aseptic, atraumatic, without tension, with a precise approximation of the wound margin and complete control of bleeding. However, it is highly probable that after resection of the auricular keloid there will be problems related precisely to tension or insufficient coverage for primary closure; For this, it is possible to choose to reconstruct the lobe or part of the auricular pavilion using local advancement, rotation or transposition flaps. At the end of the procedure, we applied in the edges of the resection a combined solution with 0.2 cc of triamcinolone and 0.8 cc of 5-FU (fluracilo).

Intralesional cryotherapy is recommended for small lesions, however, recent comparative studies have shown that intralesional cryotherapy was less effective than keloid mass resection + intralesional triamcinolone acetate infiltration therapy and combined keloid mass resection therapy. + radiotherapy [16]. For these reasons, we do not consider cryotherapy for our treatment protocol.

In order to avoid the risk of recurrence, we must also consider the aetiology of keloids related to fibroblast dysfunction. These characteristically present abnormal cell proliferation and interaction associated with hypersecretion of extracellular matrix. Taken together, all of this could be prevented after radiotherapy by controlling fibroblast proliferation, arresting the cell cycle, and inducing premature cell senescence [9].

Radiotherapy (high dose rate brachytherapy) within 6 hours after surgical resection is essential in the proposed protocol with a dose of 15 Gy in 3 fractions to prevent recurrence in 73-92% of cases, inhibiting the proliferation of the fibroblasts. Bisbal presents a 4% recurrence with the use of surgery followed by the application of brachytherapy and external radiotherapy (18). Kovalic (19), Escarmant (20) and Ollstein (21) report recurrences of 21 to 27% in longer-term follow-ups. [18-23]. The risk of carcinogenesis attributable to radiotherapy for the management of keloids is very low when the surrounding tissues, including the thyroid gland and mammary glands, are adequately protected. Therefore, it is an acceptable modality as a treatment [22]. As multiple reviews describe that indicate that surgery followed by radiotherapy provides acceptable recurrence rates, a clear definition of keloid recurrence is not specified according to clinical studies [24]. In our study we used the definition evaluation of keloid recurrence proposed by Viani, et al. 2009 [15]. The reappearance or not of the keloid or keloid mass in all or part of the treatment area was evaluated.

On the other hand, pressotherapy is based on the principle of inducing local tissue hypoxia, reducing the proliferation of fibroblasts and the synthesis of collagen. For this to be effective, a pressure between 24-30 mmHg must be generated. In our treatment protocol we implement a thermo-moldable acrylic splint (Acuaplast®). Pressotherapy has a multifactorial mechanism of action, not definitively clarified, but it also involves rearrangement of collagen fibers and a decrease in the number of fibroblasts [23].

The use of silicone on any type of scar is recommended, as it promotes correct healing, apparently by increasing tissue hydration [20], although its application on the ear and face reliefs is difficult, we used silicone gel instead of silicone sheet.

Intralesional corticosteroids are the most used non-surgical treatment for keloids. Intralesional triamcinolone acetate 10 – 40 mg/dl induces keloid regression through several described mechanisms such as: suppression of dermal inflammation, reduction of oxygen supply to the wound bed through vasoconstriction, and antimitotic activity. of keratinocytes and fibroblasts [25]. There are studies that show that monotherapy with intralesional triamcinolone acetate is associated with a higher rate of recurrence and side effects compared to combined therapies. A reduction in side effects has been reported in the combination therapy of triamcinolone + (5-flu) [26]. The association of a corticosteroid such as triamcinolone acetate with a pyrimidine derivative (chemotherapeutic agent) such as 5-fluorouracil, in our protocol is based on the enhanced effect of suppressing fibroblast proliferation. Triamcinolone suppresses cell proliferation and induces G1 cell cycle arrest, while 5-fluorouracil induces G2 cell cycle arrest and apoptosis.

Conclusion

At present, there is little agreement among the medical community on the best treatment modality for keloids. In our study, the treatment protocol for keloids of the ear has considerably reduced recurrence in our Plastic Surgery Department. Of the 18 patients registered with keloids of the auricular pavilion, we obtained a result without recurrences. This protocol consists of 4 stages. First stage: surgical resection of the keloid mass and intraoperative infiltration with a combined solution of triamcinolone and 5-FU. Second stage: radiotherapy (high dose rate brachytherapy). Third stage: pressotherapy, application of silicone gel, and finally the fourth stage with intralesional infiltration of triamcinolone + 5-fluorouracil. It is a safe protocol that presented only minor complications, such as skin thinning,

pigmentation changes, and telangiectasias. The combined therapy proposed in our protocol was shown to produce superior results than the monotherapies described in some literatures.

This modality of treatment protocol is applicable in a special way for those patients with keloid recurrences due to previous frustrated treatment and for those patients who debut with keloids in the ear region.

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