Abstract. Background: Several treatments are available to treat the keloid scar. Keloids have the tendency to recur after surgical removal and new treatments for keloid scars include radiotherapy, cryotherapy or compressive therapy. Topical treatments have been also used to treat this pathology, such as injections or medical device applications. Case Report: A 33-year-old man came to our attention and we treated him for a keloid scar located between the ear’s helical tubercle and the ante-helix upper root of the left ear. This keloid arose 20 years earlier following a bilateral otoplasty. We proposed an association therapy using a non-cross-linked hyaluronic acid and cortisone. Conclusion: The associated treatment was able to determine a complete resolution of the keloid without recurrence several months later.

The term keloid is a Greek word that means, “crab claw”. Macroscopically, a keloid appears as a hard, lumpy lesion, fixed on underlying tissue. It is different from a hypertrophic scar because it infiltrates the surrounding tissues and extends out of the edges of the wound. Keloids do not reach a spontaneous remission with time (1, 2). Itching or pain on palpation can be a symptom of a keloid. Hyper vascularization may be another sign of a keloid (3). A keloid rarely occurs in the absence of specific trauma, but may occur a few days, months or years after trauma (4).

Keloid histology appears as a structure rich in specific fibrocytes, called "myo-fibrocytes", which are several, concentric and organized parallel to the skin surface in vortexes and knots. Keloids usually recur (45% to 100%) after elective surgical treatments (1, 3). New therapies can be used post-surgery, such as radiotherapy, cryotherapy or compressive treatment (1, 5-8). Other topical treatments have been used to treat this pathology, such as injections or medical device applications (9-15).

In this case report, I describe a novel therapy that I have used successfully to treat an ear keloid for the past 15 years.

Pathological Mechanisms

Many studies have been conducted to identify the origin of keloids. Keloid has a macroscopic structure different from hypertrophic scar and this difference is demonstrated in its histological appearance. The key difference is that keloids are invasive to the surrounding tissues and extrude from the edges of the wound. The consistency of a keloid and hypertrophic scar can sometimes be similar, although the vertical growth of the keloid is often most abundant than hypertrophic scars. Other macroscopic characteristics of keloids are represented by the hardness, the lack of movement on the underlying tissues and the presence of hyper-vascularization. Studies report that 46-86% of keloids are associated to symptoms, such as itching and pain (1-5).

Keloids occur in genetically predisposed individuals after skin trauma, that can originate from infection, burn or surgery. Recent studies have shown that an increase in the skin pH (16) is able to negatively affect healing of wounds and encourage keloid formation, even in subjects not genetically predisposed.

Keloids can appear in all races, except for albinos, and the highest incidence is found in African and highly-pigmented populations where the keloid formation after trauma reaches 16% of the population (3). Recent studies have suggested that this association with pigmented skin and keloid formation may be linked to the interaction between melanocytes and fibroblasts (17). Keloid onset in one anatomical area rather than another is related to the high number of melanocytes present in the area in which it occurs (17). The upper chest, neck and ear lobes are the areas in which keloids arise most commonly. This is followed by limbs and then around the ears (9% of cases) (3). In addition to Fitzpatrick classes V and VI, individuals with genetic mutations on chromosomes 2q23 and 7p11 are more predisposed to the formation of keloids.
keloids (3, 5). Hormonal stimuli are also able to influence the onset of keloids, which is thought to explain the frequency of keloids in adolescence and at the start of menopause, as demonstrated by several studies (1). The mechanisms involved in the formation of a keloid are related to cytokine excess and the consequent over-production of transforming growth factor-beta (TGFβ), which promotes the growth and reproduction of fibroblasts. This over-stimulation is also supported by mast cells' actions that are also able to increase fibroblast proliferation (5). This increase in fibroblasts (also called myo-fibroblasts) production is also able to over-activate their capacity to synthesize the extracellular matrix, so the fibroblasts are both more numerous and more productive. A hyperactive inflammatory mechanism increases the pH and consequentially increases the risk of keloid formation (5, 7, 17). Changes in the hormonal balance also has an influence over the regulation of inflammation and pH variations (18), which may provide a potential explanation for the higher incidence of keloids in adolescents and in menopausal women.

All these factors contribute to keloid formation, which histologically appears like fibrous tissue with collagen fibres that are lying haphazardly connected in loose sheets and are randomly oriented on the epithelial surface (4). Myo-fibroblasts, that replace the fibroblasts in keloid scar, are different for their cytoplasmic microfilament bundles with nuclear indentations and cell-to-cell or cell-to-stroma connections (1).

Case Report

A 33-year-old man who came to our attention for a keloid scar located between the ear’s helical tubercle and the antihelix upper root of the left ear (Figure 1). This keloid arose 20 years earlier following a bilateral otoplasty.

Post-surgery evolution included normal wound healing during the first 7 days and, on the tenth day, a local infection of one suture of cartilage (localized abscess) – an intracartilaginous point- occurred. The patient underwent systemic antibiotic therapy and point removal. An injection of cortisone (2 mg of Bentelan) was performed, directed at the source of the infection. This treatment was performed twice within 20 days as suggested. Thirty-five days after the last injection, despite continued treatment, a keloid (about 1 cm with the shape of a grain of millet) developed again in the infected area.

Sixty days after, due to the persistence of the lesion, an otolaryngologist tried a surgical excision of the keloid, but a keloid recurred between the helix and upper root of the ante helix at the third middle ear level (diameter of about 2.5 cm), causing a skin synechia between these two structures. No other treatment was recommended after this new problem developed.

In 2015, the patient came to our attention and requested treatment for a keloid 20 years after its onset. The patient refused laser treatment. We proposed therapeutic injections of cortisone and non-cross-linked hyaluronic acid injections (Restylane Vital®; Galderma Laboratories, L.P14501 North Freeway Fort Worth, TX 76177 USA).

We obtained the patient’s consent before treatment and started the treatment with methylprednisolone acetate 40 mg (1 ml was injected using a 30 gauge needle). We made the infiltration of the keloid and the surrounding area between the scaphoid fossa, helix, tubercle headset and ante helix root top using a 30 gauge needle. The infiltration technique was important to prevent cartilage necrosis and avoid inter-cartilaginous cortisone infiltration. The needle, same used to make infiltration, was used previously to elevate the adhesion area between the keloid and cartilage (Figure 2), after which cortisone was released in a retrograde manner. We also carried out several infiltrations in the central portion of the keloid. Cortisone infiltrations were carried out with the following therapeutic scheme: 40 mg at T0, T15 40 mg, 30 mg at T30 and 20 mg at T60. During the intercurrent T period between one cortisone infiltration and the other, an
infiltration with 0.8 ml Restylan Vital to T7, T21, and T45 was made in inter- and peri-keloid areas (Table I).

After each injection, the patient used topical therapy of Dermatix® (Valeant Pharmaceuticals International, Bridgewater, NJ, USA) with 1 daily application only during the first 30 days of therapy. No compressive medication was applied.

Thirty days after the last cortisone infiltration, treatment was suspended to observe the lesion evolution. Thirty-five days after the end of treatment, the keloid acquired a soft consistency, was reduced by 40% and the skin synechia became smaller (Figure 3).

We repeated corticosteroid treatment again after the first one effectuated before with this type of treatment: 40 mg to T0, 30 mg to T20, and T50 to 20 mg (Table II).

We performed 2 inter- and peri-keloid infiltration treatments with 0.8 ml of non-cross-linked hyaluronic acid (Restylane Vital®) between cortisone therapy sessions, and precisely at T15 and T45, even during the second session treatment with cortisone.

Synechia disappeared and the keloid was reabsorbed at 15 days after the last cortisone infiltration (Figure 4). The patient did not show any recurrence of the lesion at the 6-month and 12-month follow-up visits.

Discussion

The combination treatment with hyaluronic-acid and cortisone is frequently used in orthopaedics to treat inflammatory tendon disease (18). Recent studies performed in vivo and in vitro have clarified the action mechanism of this therapy; cortisone is able to reduce the proliferation of fibroblasts in a dose-dependent manner, while hyaluronic acid is able to reduce inflammation by acting on prostaglandin 2 secretions (18).

The ability of non-cross-linked hyaluronic acid to enhance the extracellular matrix of the dermis, when used regularly for a minimum of 3 consecutive sessions with a maximum of 30 days distance between injections, is also widely known (19). Tendons are composed of fibroblasts, named "tenocytes", that are arranged linearly with little amorphous substance. Keloids are rich in fibrocytes and coarse connective bundles that increase the texture and scarring.

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making it look more similar to a "tendon" structure. Based on the structural similarity between the two tissues, we predict that the combination of cortisone and Restylane Vital® would induce keloid regression.

Treatment sessions alternated between cortisone and hyaluronic acid every 15 days during the entire treatment period. Treatment could be able to balance the turnover of fibroblasts, evoking a wound healing mechanism with no more pathological activity and determining keloid involution. The accuracy of the injection method, especially in putting hyaluronic acid directly into the dermis, was definitely an important aspect of this therapy.

Different treatments are currently available to prevent keloid formations, such as topical therapies with silicone, cream with collagen or cortisone. These methods, unfortunately, can only be used during the remodelling phase of wound healing (2 years after surgery). It is possible to use compression methods to treat keloids in the areas where it is anatomically suitable, the ear level for example, in subjects who are predisposed to keloid formation. Treatments using silicone or compression (12-14) are able to determine a tissue hypo-oxygenation and to reduce, in this way, both the vascularization and the regenerative phenomena at a tissue level. Pharmacological treatment using cortisone injections directly into the dermis to reduce inflammatory phenomena is carried out during the first 6 months after surgery to avoid and prevent keloid formation (6-11). If the keloid recurs, laser therapy can be effective (5, 7, 14). Alternatively, surgical resection with careful post-procedure monitoring of wound healing during the recovery time may be effective (6, 7). It is possible to use cryotherapy as a single treatment or in combination with surgery/radiation therapy (5, 7). The latest generation of treatments, which are still in an experimental phase, are represented by interferon bleomycin or 5-fluorouracil injections (5, 12, 13).

In this case report, we used a combination of cortisone and Restylane Vital® because the patient refused additional surgical treatment or laser therapy (15). Even if a keloid was developed several years previously, repeated treatments carried out with various doses of cortisone associated with non-cross-linked hyaluronic acid injections reach out the complete resolution of the lesion. The accuracy and precision of the dissection method, the extended infiltration, the dose adjustment according to lesion responses and constant repetition of therapy produced a satisfactory result after a period of about 6 months.

The author suggests that the position (20) in which the keloid arose was helpful during injection treatment to keep the inflammatory phenomena under control and treatment in place without any dispersion of cortisone and hyaluronic acid. Also, due to the thinness of the skin in this area, it was easier to identify the dermis and ensure that the infiltration was not in contact with the ear cartilage. If cortisone is injected in a place that is rich in subcutaneous tissue, the drug diffusion into the tissue does not permit specific action in the area that has to be treated, thus decreasing the chances of success.

In conclusion I want to summarize disadvantages and advantages of my technique. Probably, the most important disadvantage is related to the price of non-cross-linked hyaluronic acid used for the treatment, this is not registered as a drug, so the patient have to pay by himself the price of the treatment. Less important disadvantages are related to the repeated infiltrations necessary to obtain the results; this problem is also related to other techniques, not only to the injective ones but also to the laser use. The advantages of this technique are several, first of all the physiological restoration of cells balance thanks to the double effect anti-inflammatory and stimulating of the treatment. Although
several infiltrations are necessary. I used a 25 gauge needle to inject cortisone and a 30 gauge needle to inject the non-cross-linked hyaluronic acid, that permits the reduction of traumatisms and less inflammatory answers, this is opposite, for example, at the surgery treatment where an important inflammatory answer is always present. The retrograde infiltration technique is able to destroy the internal structure of the keloid and, the releasing of non-cross-linked hyaluronic acid after this needle passage, modify the nature of the cells so to restore the normal histology of the skin; other techniques as criotherapy or radiotherapy are able to destroy keloid’s structure only and determines fibrotic rearrangements of skin cells without a real regeneration of the tissue. Finally, the technique is able to increase the cellularity of the lesion and to improve the quality of the vascularization in the treated area, thanks to the regenerative ability of non-cross-linked hyaluronic acid, without risk of tissue necrosis that could happen using compressive devices.

I, therefore, emphasize, as conclusion of this case report, that, although drug dosages and number of treatments are important, their prolonged duration in time (6-11), area in which treatment is carried out and anatomy of the area are important as well (20). Pharmacological studies, to develop more viscous substances, and the association between cortisone and hyaluronic acid for injection use, could open new horizons in the development of innovative treatments of keloids.

References


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