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Keloids: combined therapeutic solutions

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Background. **Keloids are, pathological painful scars, prominent and proliferating beyond the original wound shape, which recur after surgical excision. Their aetiology is much debated, and many hypotheses have been put forward. No single known cause exists, but many factors that modify and increase the normal wound-healing process have been considered as probably involved in the genesis of keloids; for this reason many different therapeutic approaches directed towards each of the causing factors are used.**

Methods. **Considering the different therapeutic strategies and the physiopathological mechanisms they contrast, we found the most promising solution in the association of surgery, postoperative radiotherapy and compressive dressings with silicone gel sheeting.**

Results. **Seven out of 11 keloids (9 patients) treated in this way did not recur after an observation period of 2 months - 3 years; 1 patient developed a hypertrophic scar 18 months after surgery, that underwent regression after a 3-month treatment with silicone gel sheeting; 3 keloids recurred 3-5 months after their excision.**

Conclusion. **Considering the results obtained in this limited number of patients, we believe that the association of surgery, radiotherapy and compressive silicone dressings represents a possible combined treatment modality that deserves some consideration, and that needs to be verified on greater populations in further studies.**

KEY WORDS: Keloid, diagnosis - Keloid, surgery - Keloid, radiotherapy - Silicone gels, therapeutic use.

Keloids are pathological metaplastic scars, characterised by excessive and anarchic collagen deposits that give them a raised shape, and make them grow beyond the margins of the original wound. They cause symptoms like pain and itching and tend to recur after surgical excision. Their aetiopathogenesis is obscure, although if many predisposing factors have been detected. The therapeutic approach can be pharmacological (steroids, retinoids), mechanical (compressive dressings, silicone gel sheeting), surgical, radiotherapeutic. None of these procedures is effective on its own, because they show very changeable results. For this reason, two or more methods are often associated.[1, 2]

The purpose of our study was to verify the effectiveness of the therapeutic association of surgery, radiotherapy and silicone gel sheeting dressings.

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Materials and methods

Over a period of 6 years (1997-2001), 9 patients affected by 11 keloids were admitted to a therapeutic protocol consisting of surgical excision, followed by radiotherapy and compressive silicone gel sheeting dressings.

The patients were all caucasians, 5 males and 4 females. Their average age was 28.1 years (aged 12 to 55).

The anatomical regions and causes of onset of keloids are reported in Table I.

Table II shows the dimensional parameters relative to length, width and projection of the keloids from the cutaneous surface: they were on average e 1.5 cm wide, 3.32 cm long, and 0.52 cm high.

The average time of onset after the traumatic event was 8 months (2 to 12 months).

All the patients reported pain (light to severe), itching, paresthesias.

Before the operation each patient was sent to the Radiotherapist for a preoperative examination. In this examination the projection of the keloid was measured and the dose and energy of the electron beam necessary for the treatment were consequently decided. Each patient was adequately informed of the kind and modalities of treatment he/she was to receive, and on the absence of any biological risk deriving from the electron beam.[3]

Each patient signed a document stating her/his assent to the sanitary procedure (Informed Assent: art. 31 and 32 of the Italian New Medical Deontologic Code).

hypertrophic scar developed (11.1% of the patients: 1 out of 9).

Over a period of 5 months to 3 years after the operation, in the successful cases all the scars looked flat, linear, normotrophic, pale and were not painful (keloids no. 1, 2, 3, 4, 5, 8, 11).

In 1 of the unsuccessful cases (keloid no. 6) a new, painful keloid recurred 5 months after surgery and 1 year later the situation looked unvaried (the patient admitted that he had followed the prescribed therapy with silicone gel sheeting and gel of allantoin and sulphomucopolysaccharides (Sameplast gel®) only for 2 months).

Keloids no. 9 and 10 (patient H) recurred 3 months after surgery, and appeared bigger than the previous ones.

In 1 case (keloid no. 7, Figure 1) a hypertrophic scar developed 18 months after surgery (hyperemic cord, raised, slightly painful); after a 3-month treatment with compressive silicone gel sheeting dressings and circular massages with a gel with allantoin and sulphomucopolysaccharides (Sameplast gel®), the scar turned paler and completely flattened (Figure 2).

Discussion

Keloids are metaplastic scars, characterised by an excessive and anarchic collagen deposit proliferating beyond the limits of the original wound and causing different symptoms (pain, itching, paresthesias, aesthetic problems). Moreover, they are prone to recurrence after excision.[1, 2, 7-10] The anatomical regions mostly affected by keloids are the shoulders, the presternal region, the auricolar lobes, the cheeks and the neck.[11]

Their aetiopathogenesis is obscure, although many predisposing factors have been detected. At any rate, keloids represent a "derailment" from the normal wound-healing process: alterations in each step of this process have been reported in the onset of pathological scars.[12-37]

Considering all the hypotheses advanced on keloid genesis and all the different treatment modalities suggested, we found the most promising solution in the association of surgery, radiotherapy and silicone compressive dressings.

Surgery eliminates the keloid, but at the same time represents a trauma, recruits and activates cells and growth factors of the wound-healing process. Therefore, it can cause the reactivation of one or more of the pathological steps of keloid formation. Results on simple excision of keloids reported in the literature are very different: recurrences are reported in 45-100% of the cases.[37-40] For this reason it is necessary to associate other therapies with surgery, in order to inhibit the individual predisposition to recurrence.[38]

Radiotherapy has been reported as successful on its own in 56% of cases and in association with previous surgical excision in 63-80% of cases.[3, 39, 41] Radiotherapy can be applied immediately after surgical excision, in order to oppose as soon as possible those pathological mechanisms that, left undisturbed, could generate another keloid. Its effects are directed towards the margins of surgical excision, that is, towards the tissues that immediately surround the keloid that could originate. The electrons of the incident beam, interacting with DNA of the cells they pass through, cause their necrosis or lesions. This reduces their proliferation. Since fractioning would damage a greater number of cells, a single dose was applied in order to obtain a delicate balance. In so doing, the healing process is inhibited in its pathological excesses, but not in its necessary and essential physiological function of healing the surgical wound. The total maximal dose of 4 Gy is effective, and also low enough to prevent recurrence of side effects in the patients.[3-6]

Radiotherapy, therefore, is seen as the first step in the process of wound-healing, in that it limits the proliferation of the cells primarily involved in the acute inflammatory response (neutrophils, monocytes and resident macrophages), and blocks their production of growth factors and chemotactic cytokines. These would recruit and activate fibroblasts which disorderly produce collagen.[3] Moreover, radiotherapy also hits the skin around the scar: this is an advantage, since keratinocytes are probably involved in keloid fibroblast proliferation, through paracrine or epithelial-mesenchymal signaling.[37]

Compressive dressings with silicone gel sheeting, associated with circular massages with a specific topic preparation, act over the maturation and organisation of the scar and interfere with collagen synthesis and cross-linking.[42, 43] In fact, pressure reduces tension within the scar and causes ischemia, inducing a reduction of cellular metabolism, of the number of fibroblasts and of the cohesion among collagen fibrils, and an increase of collagenasic activity in the wound.[29, 42] Silicone gel sheets determine hypoxia, contributing to the ischemic effect of compression, and also a greater hydration and elasticity of the wound (increased by the massages with allantoin and sulphomucopolysaccharides gel, Sameplast gel®).[1, 2, 43, 44] Postsurgical application of silicone dressings are reported to prevent keloid recurrences in 75-85% of cases.[2, 43]

Single therapies are quite ineffective in the treatment of keloids; therefore, 2 or more methods are often associated.[2] Results reported in the literature regard only the association of surgery and radiotherapy (successful in 63-80% of cases),[2, 3, 41] or of surgery and silicone gel sheeting (successful in 75-85% of cases),[2, 43] but not the association of all the three therapeutic modalities.

In our study only patients affected by real keloids (not hypertrophic scars) were selected. The keloids caused them severe aesthetic and/or physical symptoms, and had never been treated before. Moreover, the patients had to be strongly motivated to go through all the steps of the therapy (compliance is very important for the efficacy of the treatment, above all in the postsurgical period). As far as radiotherapy is concerned, other standards had to be considered: the patient's age had to be over infancy (very young organisms grow rapidly and their cells undergo frequent mythosis; they are therefore rather susceptible to radiation-induced cellular transformation); moreover, the anatomical region of the keloid had to be safe (*e.g.* we did not admit fertile females with keloids in their lower abdominal quadrants). The electron beam is accurately collimated, so that it does not penetrate into the tissues beyond a limit identified according to the keloid thickness.[3] Nevertheless, we considered it safer, from ethical, medical and legal points of view, not to expose our patients' health or reproductive function to even the minimal risk).

Among the recurrence percentage of our series (27.27%),

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