

ACTASDermo-Sifiliográficas





ORIGINAL ARTICLE

Surgical Treatment of Relapsing Keloid of the Pinna by Fillet Flap

- P. Valerón-Almazán, L. Dehesa-García, J. Vilar-Alejo, J. Domínguez-Silva,
- J. Gómez-Duaso, and G. Carretero-Hernández*

Servicio de Dermatología, Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas de Gran Canaria, Spain

Manuscript received May 4, 2009; accepted for publication September 3, 2009

KEYWORDS

Flap; Pinna; Keloid; Relapsing

Abstract

Background and objectives: Keloid scars occur when, compared to normal healing, there is excessive formation of collagen after skin wounds or burns. Different treatments have been tried, though no particular one has been shown to be superior. The objective of this study was to assess the usefulness of the surgical technique originally described as keloid fillet flap in the management of relapsing keloids of the pinna.

Material and methods: The study included 10 patients (8 men, 9 white and 1 black) with a keloid on the retroauricular region or earlobe of more than 1 year duration, who had undergone previous treatment (surgery and topical or injected corticosteroids) without a good outcome or with relapse, and who had not received any treatment in the previous 6 months.

Results: Five patients were treated with a fillet flap procedure only, while the other 5, in addition to the procedure, also applied 5% imiquimod cream 5 times a week for 1 to 3 months. In 4 patients, no relapse was observed after the intervention. Two patients had partial flap necrosis, with subsequent partial relapse in one of these. Eighty percent reported the outcome of the procedure as good or excellent.

Conclusion: We achieved a response rate of 40% in the treatment of relapsing keloid of the pinna by a fillet flap procedure. This may be an alternative within the therapeutic arsenal for the treatment of relapsing keloid of the pinna, given that it does not require extensive resources and the skills needed to perform the procedure can be quickly acquired.

© 2009 Elsevier España, S.L. and AEDV. All rights reserved.

236 P. Valerón-Almazán et al

PALABRAS CLAVE

Colgajo; Auricular; Queloide; Recidivante

Tratamiento quirúrgico del queloide recidivante de pabellón auricular mediante «colgajo en filete»

Resumen

Introducción y objetivos: El queloide se caracteriza por la formación excesiva de colágeno respecto a la cicatrización normal y puede aparecer de forma secundaria tras una herida o quemadura cutánea. Para su corrección se han ensayado diversos tratamientos, sin que ninguno haya demostrado su superioridad. El objetivo de este estudio es valorar la utilidad de la técnica quirúrgica originalmente descrita como keloid fillet flap (colgajo «en filete») para el tratamiento de queloides auriculares recidivantes.

Material y métodos: Se seleccionaron diez pacientes (ocho varones, nueve de raza blanca, uno de raza negra) con queloide retroauricular o de lóbulo recidivante de más de un año de evolución, que habían recibido tratamiento previo (cirugía y corticoides tópicos o en infiltración) sin resultado o con recidiva, y que no habían recibido ningún tipo de tratamiento en los últimos seis meses.

Resultados: Cinco pacientes fueron tratados quirúrgicamente solo con colgajo «en filete» y otros cinco con colgajo e imiquimod crema al 5% cinco veces por semana durante uno a tres meses. En cuatro pacientes no se apreció recidiva tras la intervención. Dos pacientes presentaron necrosis parcial del colgajo, uno de los cuales desarrolló recidiva parcial de la lesión. El 80% calificó el resultado de la intervención como bueno o excelente.

Conclusiones: Hemos conseguido un 40% de respuesta en el tratamiento del queloide auricular recidivante mediante la realización de colgajo «en filete». Este puede representar una alternativa dentro del arsenal terapéutico disponible para el tratamiento del queloide auricular recidivante, dado que no necesita de grandes medios y puede realizarse después de un entrenamiento mínimo.

© 2009 Elsevier España, S.L. y AEDV. Todos los derechos reservados.

Introduction

Keloid (from the Greek chele, crustacean claws) scar tissue appears following a skin wound or burn and is characterized by excess formation of collagen. The phenomenon of excess scarring in some wounds was first described by Jean Louis Alibert, who, in 1817, proposed the term cheloide, thereby differentiating it from neoplastic growth.² Several mechanisms have been implicated in the formation of keloid tissue, including growth factor abnormalities, defective collagen turnover, changes in the orientation of collagen fibers due to tension, immune system dysfunction, or hypersensitivity to sebum, etc,3 although none of these independently and unequivocally explains the formation of keloid scars in all cases. Moreover, they are known to be more frequent among black individuals, 4,5 show familial clustering in some cases, have a tendency to appear in young individuals and during active stages of life,6 and show a preference for some anatomical locations.7

Their characteristic exuberance and capacity for relapse, which differentiate them from hypertrophic scars, 8 make these scars one of the most frustrating entities in skin surgery. Many treatments have been carried out in an attempt to correct this condition, including simple excision, intralesional injection of corticosteroids, application of pressure, radiation therapy, application of silicone gel or patches, laser treatment, 5-fluorouracil, retinoids, and interferon (IFN). 3 However, none has been shown to be superior or to guarantee resolution of the condition or prevent relapse.

Keloid of the pinna has become increasingly common due to the current popularity of piercing and has traditionally received the same treatment as keloid scars on other areas of the body, with similarly discouraging results. Added to this therapeutic challenge is the evidence that keloid scars on this part of the body have important cosmetic implications that can considerably curtail the quality of life of these patients.

Due to the increasingly frequent referral of patients with this problem, we decided to re-evaluate the treatment. Out of the different alternatives proposed for trying to reduce the capacity for relapse shown by conventional keloid surgery, 9-12 we chose the technique that was initially proposed, under a different name, by Lee et al 9 and, later, by Kim et al, 10 and known to us as the fillet flap. We carried out a trial of this technique in a small group of patients with recurrent keloid of the pinna.

Materials and Methods

Patients

A total of 10 patients (8 men and 2 women; 9 white and 1 black) were seen at the dermatology department of Doctor Negrín University Hospital, Gran Canaria, Spain between December 2006 and April 2008 with keloid scars behind the pinna or on the earlobe; the scars had developed more than a year earlier and were stable. The patients had received previous surgical treatment on several occasions (a minimum of 2 and a maximum of 4 operations) and an infiltration of corticosteroids, with unacceptable results or relapse; retreatment and alternative treatments had been

ruled out in these patients (patients referred from other departments or colleagues).

The following exclusion criteria were used: having received treatment for the keloid (of any type) in the 6 previous months, being under the age of majority, being pregnant or breastfeeding, having allergies to anesthetics, or being likely to fail to adhere to any additional treatment or attend clinical follow-up.

The therapeutic objective was to achieve a rate of at least 50% complete excisions with no relapse at 12 months. Relapse was considered to be postoperative recurrence of growing or persistently symptomatic scar tissue. The demographic data of the patients are summarized in Table 1. We also carried out a subjective evaluation survey of the patients in which patients rated the level of personal satisfaction after the procedure and the final result (poor, middling, good, or excellent).

Surgical Protocol

Following administration of local anesthesia (lidocaine, 1% with epinephrine 1:100 000 buffered with sodium bicarbonate), we performed an incision in the skin, following the margin of the keloid, to detach the epidermis and superficial dermis of the keloid, enucleate the keloid, and subsequently suture the fillet obtained using Ethilon 5/0 or 6/0 (Figures 1 and 2). The wounds were treated once daily with 2% topical mupirocin, the sutures were removed after 7 days, and the wound was assessed and photographed at 30, 90, 180, and 360 days, or on demand, depending on the start of relapse of the keloid in the following weeks or months. Patients in whom surgery had been performed in the area on more than 2 previous occasions were treated with 5% imiguimod cream once daily, from Monday to Friday, for between 1 and 3 months; similar treatment was used subsequently in patients with evidence of relapse.

Table 1 Patient Clinical Data

Sex	
Male	8
Female	2
Race	
White	9
Black	1
Age, median (range), y	22-71 (33.2)
Cause of keloid	
Piercing	8
Otoplasty	1
Trauma	1
Previous Treatment	
Simple surgery (on at least	10
2 previous occasions)	
Topical corticosteroids	1
Intralesional corticosteroids	6



Figure 1 Detail of the surgical technique (patient 2). A, Preoperative appearance of the keloid. B, Flap obtained after dissecting the keloid core. C and D, Result immediately after surgery.



Figure 2 Detail of the surgical technique and postsurgical course leading to partial relapse (patient 9). A, Preoperative appearance of the keloid and definition of the flap to be used. B, Appearance of the fillet flap. C, Result of the technique immediately after surgery. D, Partial relapse after 5 months of follow-up.

Results

Five patients were treated with fillet-flap surgery alone and 5 with fillet flap and topical imiquimod 5 days a week for between 1 and 3 months. Patient follow-up was carried

out for between 12 and 28 months (mean follow-up period, 18.2 months). At the time of writing, no relapse had been observed in 4 of the 10 patients (Figure 3). Two patients presented partial flap necrosis (Figures 4 and 5); one of



Figure 3 A, Detail of the course of patient 2 at 25 months following fillet flap surgery. B, Detail of the course of patient 10 at 12 months following fillet flap surgery.

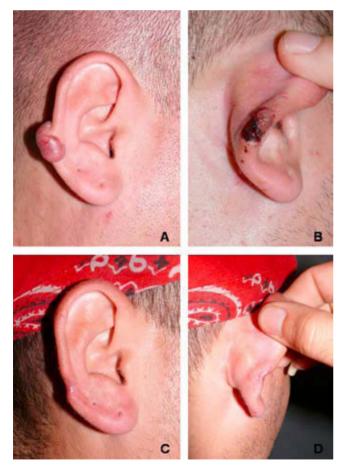


Figure 4 Postsurgical course leading partial flap necrosis without relapse of the keloid (patient 10). A, Preoperative appearance of the lesion. B, Partial flap necrosis 11 days after surgery. C and D, Final result of surgery after 4 months of follow-up.



Figure 5 Postsurgical course leading to partial flap necrosis and subsequent partial relapse (patient 5). A, Preoperative appearance of the keloid. B, Result of the technique immediately after surgery. C, Appearance of the flap 7 days after surgery. D, Final result of surgery after 8 months of follow-up.

these patients subsequently presented partial relapse of the keloid lesion 4 months after the fillet flap procedure. The result of the operation was rated as good or excellent by 80% of patients. The data obtained are summarized in Table 2.

Discussion

No treatment for keloid scars is currently available that guarantees good results in all cases. Surgical excision of keloids is usually accompanied by relapse in between 45% and 100% of cases, 13 in some cases even recurring in a more extreme form that exceeds the limits of the lesion being treated. Adjuvant treatment (radiation therapy, intralesional corticosteroids, 5% topical imiquimod, cryotherapy, laser treatment, intralesional interferon, etc) somewhat improves the percentage of relapses, although it may also lead to an even larger keloid. In practice, the approach to this condition very often involves a combined treatment that includes more than 1 of the above techniques. One of the most commonly used treatments combines surgical excision with intralesional injection of corticosteroids; this combination has been reported to reduce the rate of relapse by between 3% and 25%. 14,15

 Table 2
 Data and Results of the Series of Patients Treated

Fillet flap+imiquimod 5% 2 Fillet flap Fillet flap-imiquimod 5% 2.5 Fillet flap Fillet flap Fillet flap+imiquimod 5% 2.5		Back of earlobe Back of earlobe Back of earlobe	Fillet flap+imiquimod 5% Fillet flap		Excellent Good	4 mo	22 mo. No relapse
26 W Back of earlobe Fillet flap 71 W Back of earlobe Fillet flap 84 W Back of earlobe Fillet flap 85 W Back of earlobe Fillet flap 86 W Back of earlobe Fillet flap 87 W Back of earlobe Fillet flap+imiquimod 5% 1.5 88 W Back of earlobe Fillet flap+imiquimod 5% 2 89 W Back of pinna Fillet flap+imiquimod 5% 2 80 W Back of pinna Fillet flap+imiquimod 5% 2.5 80 W Back of pinna Fillet flap+imiquimod 5% 2.5 81 W Back of pinna Fillet flap+imiquimod 5% 2.5 82 W Back of pinna Fillet flap+imiquimod 5% 2.5		Back of earlobe Back of earlobe	Fillet flap		Good		25 mo No related
71 W Back of earlobe Fillet flap+imiquimod 5% 2.5 28 W Back of earlobe Fillet flap 22 W Back of earlobe Fillet flap+imiquimod 5% 1.5 24 W Back of earlobe Fillet flap+imiquimod 5% 2 35 W Back of pinna Fillet flap+imiquimod 5% 2 37 W Back of pinna Fillet flap+imiquimod 5% 2.5 38 W Back of pinna Fillet flap+imiquimod 5% 2.5		Back of earlobe	Fillet flantimidition 5%			9 mo	2.7 III.O. INO I Etapse
28 W Back of earlobe Fillet flap 2.5 34 W Back of earlobe Fillet flap 2.5 22 W Back of earlobe Fillet flap+imiquimod 5% 1.5 24 W Back of earlobe Fillet flap+imiquimod 5% 2 35 W Back of pinna Fillet flap+imiquimod 5% 2.5 37 W Back of pinna Fillet flap+imiquimod 5% 2.5	•		ווובר וומלו ווווולמוווסם זיי		Good	3 mo	12 mo. Partial relapse (1 mo)
34 W Back of earlobe Fillet flap 2.5 22 W Back of earlobe Fillet flap+imiquimod 5% 1.5 24 W Back of earlobe Fillet flap+imiquimod 5% 2 35 W Back of pinna Fillet flap+imiquimod 5% 2.5 37 W Back of pinna Fillet flap+imiquimod 5% 2.5		Back of earlobe	Fillet flap	2	Middling	8 mo	28 mo. Partial relapse (10 mo)
22 W Back of earlobe Fillet flap+imiquimod 5% 1.5 24 W Back of earlobe Fillet flap+imiquimod 5% 2.5 35 W Back of pinna Fillet flap+imiquimod 5% 2.5 37 W Back of pinna Fillet flap+imiquimod 5% 2.5		Back of earlobe	Fillet flap		Excellent	4 mo	18 mo. Flap necrosis. Partial relapse (4 mo)
W Back of earlobe Fillet flap+imiquimod 5% 2 W Back of pinna Fillet flap+imiquimod 5% 2.5 W Back of pinna Fillet flap+imiquimod 5% 1.5		Back of earlobe	Fillet flap+imiquimod 5%		Good	11 mo	12 mo. No relapse
W Back of pinna Fillet flap+imiquimod 5% 2.5		Back of earlobe	Fillet flap+imiquimod 5%	2	Good	3 mo	12 mo. Partial relapse (1 mo)
1 t		Back of pinna	Fillet flap+imiquimod 5%	2.5	Good	2 mo	19 mo. Partial relapse (3 mo)
רווובר וומלי	× 7	Back of earlobe	Fillet flap	1.5	Middling	4 mo	22 mo. Partial relapse (4 mo)
10 M 26 W Back of pinna Fillet flap 2 E	M 9	Back of pinna	Fillet flap	2	Excellent	10 mo	12 mo. Partial flap necrosis. No relapse

Abbreviations: B, black; F, female; FF, fillet flap; M, male; W, white

The pathogenesis of keloid formation is still unknown and, while different hypotheses have been put forward, it is still not possible to adopt a targeted therapeutic approach. No clear evidence exists to indicate that either the medical or surgical approach is superior in terms of results. For this reason, many treatments have been proposed treatments, and this will probably continue to be the case.

Keloid of the pinna has been treated with all treatment alternatives aimed at keloid scars in any other location, with similarly discouraging results. All the patients in our study had been treated previously with surgery (all on a minimum of 2 and a maximum of 4 occasions) and most of them (60%) had been treated with intralesional corticosteroids; the previous treatments had been shown to be ineffective.

Several options for surgically treating keloid of the pinna have been used, including direct suture, healing by second intention, skin grafts, and local flaps; no comparative studies of the different techniques have been done. The anatomic complexity of the area and the variability in the form of presentation of the keloid scars (size, location, etc) are probably determining factors that make standardizing a particular surgical procedure difficult.

Reducing the tension in the suture and other specific surgical measures are known to help reduce the appearance of keloids (the classic gold-standard method in antikeloid surgery of 5As and 1B, from asepsis, atraumatic technique, absence of raw surface, avoidance of tension, accurate approximation of wound margin, and complete bleeding control), 10 so that any technique that meets these criteria would, theoretically, provide a greater likelihood of success. The surgical technique used by us, known by different names (keloid core excision or keloid fillet flap^{9,10}), meets these technical requirements and, in previous small studies, provided results that were acceptable in our opinion. Their use, therefore, provides hope. We chose to use the name fillet flap because, in our opinion, the surgical technique used is a flap technique and the use of the word excision seems excessively vague. This is a surgical technique that, as we have mentioned, meets the desired anti-keloid objectives (5A and 1B), although it does present some technical difficulties: dissecting the keloid core is sometimes difficult due to the strong adherence between the dermal and epidermal components and the skin obtained is deteriorated, either due to the surgery itself when attempting to enucleate the dermal component or by the distension caused by the growth of the keloid.

As mentioned, the flap obtained using this technique is almost completely avascular (it practically constitutes a dermal-epidermal graft obtained from the top of the keloid, although it is connected to the rest of the skin by a pedicle), so that it is, in theory, fed by the subcapsular vascular plexus. Thus, the practical use of the technique may be limited by the size of the flap as this will be subject to partial or total necrosis if the vascular plexus is not sufficient to supply it. However, some studies have suggested that it is possible to achieve flaps of considerable size. In our study, the largest flap was 2.5 cm. In 2 cases (2 and 2.5 cm), the flap suffered partial necrosis, with healing by second intention (topical imiquimod was administered

240 P. Valerón-Almazán et al

in these cases). One of these patients presented partial relapse after 4 months of follow-up. However, both patients rated the result of the operation as excellent (better result than in previous surgical interventions).

The use of 5% topical imiguimod as a complement to keloid surgery appears to be safe and may be effective at reducing the rate of relapse. 11,12,17 Martín-Galán et al 18 showed that the use of 5% imiguimod was effective at preventing relapse in 75% of surgically treated keloids after 24 weeks of follow-up. A hypothetical double-action mechanism has been proposed in which imiguimod would alter gene expression in the keloids19 and this would probably reverse both the genetic abnormalities in the keloids20 and the reduced rate of apoptosis in the keloid core.21 It may also act by inhibiting the production of collagen and glycosaminoglycans secondary to the induction of IFN-γ.²² However, it has not been conclusively shown that these proposed actions fully explain the supposed benefit. In our study, we restricted the use of imiquimod to patients who presented relapse of the lesion and patients with a history of more than 2 previous operations (5 patients in total). The use of 5% imiguimod cream may be an effective option for the use in combination treatment for keloid of the pinna, although further studies are needed that compare imiquimod with surgery as single therapy and with other adjuvant treatments.

Finally, we deemed it useful to include as part of the study data the level of patient satisfaction after surgery and not only the end result of the surgery, as this condition can limit patients' quality of life due to its unsightly appearance. In our study, 80% of patients treated with this technique expressed an acceptable level of satisfaction (good or excellent) after surgery, even though more than a third of the satisfied patients suffered a relapse.

We achieved a 40% response rate in the treatment of recurrent keloid of the pinna by fillet flap. While in some specific cases (patients with more previous surgical operation or with incipient early relapse after surgery) topical application of 5% imiguimod was added, the final percentage of good results (40%) is highly acceptable in our opinion, even though we did not achieve the figure of 50% of excisions without relapse, which we had established as the objective of the study. In our opinion, the fact that, in patients who suffered relapse (60%), the resulting keloid was smaller than the original lesion and that the level of patient satisfaction was never defined as poor is notable. We believe that the background of the patients in our study (all patients had undergone previous surgery in the same area and had received other treatments with no positive outcome and, in all cases, with relapse, sometimes even producing a lesion that was larger than the previous) determined the end result of our findings. These percentages are in line with findings by other authors.

We are aware that the final evaluation of this technique is conditioned by the fact that it is not possible to safely determine a specific length of time after which it can be stated that the keloid has not relapsed, as late relapse is well known in this condition. In order to evaluate this aspect, we included time to relapse after previous surgery in our analysis (Table 2) as a comparative measurement against the previous therapies tried in our patients. In

the earliest case, relapse occurred 2 months after the last operation and, in the latest case, after 11 months of follow-up (mean length of time after which relapse occurred following previous surgery, 5.5 months). All patients in whom relapse of the keloid was not observed after fillet flap surgery have exceeded the relapse time they experienced following the previous surgery. When considering the benefits of this or other therapeutic options, we believe that it is necessary to include the level of patient satisfaction in the analysis, as this is a condition with considerable cosmetic repercussions.

With these limitations in mind, we believe that the fillet flap technique may be an acceptable option to consider as part of the therapeutic arsenal available for the treatment of keloid of the pinna, as it does not require substantial resources or extensive training.

Nevertheless, despite having almost reached the therapeutic target set for this study, we believe that the result of the technique needs to be improved, either by means of simultaneous or sequential combination of other therapies (especially therapies that modulate collagen synthesis) or by correct selection of the type of keloid (lobular compared to multilobular, location on the pinna, etc); this would allow us to reduce recurrence rates and make the technique a good choice for treating this difficult skin condition.

In conclusion, keloid continues to be a therapeutic challenge, particularly in the pinna, given its increase due to the growing widespread use of piercing in the Spanish population. Keloid of the pinna tends to recur frequently and has a considerable impact on patients' quality of life. Thus, any attempt to achieve partial or total improvement in an acceptable percentage of patients with this condition is of major interest. We believe that the results obtained in our small number of patients allow us to consider this form of treatment as an acceptable and useful option in some cases of recurrent keloid of the pinna.

Conflicts of Interest

The authors declare no conflicts of interest.

References

- Cohen IK, Keiser HR, Sjoerdsma A. Collagen synthesis in human keloid and hypertrophic scars. Surg Forum. 1971;22:488-9.
- Alibert JLM. Quelques recherches sur la cheloide. Mem Soc Med d'Emul. 1817;744 [cited by Lee Y, Minn KW, Baek RM, Hong JJ. A new surgical treatment of keloid: keloid core excision. Ann Plast Surg. 2001;46:135-40].
- Al-Attar A, Mess S, Thomassen JM, Kauffman CL, Davison SP. Keloid pathogenesis and treatment. Plast Reconstr Surg. 2006:117:286-300.
- 4. Oluwasanmi JO. Keloids in the African. Clin Plast Surg. 1974;1: 79-95.
- Bayat A, Arscott G, Ouiev WER, Ferguson MWJ, McGrouther DA. Description of site-specific morphology of keloid phenotypes in an Afrocaribbean population. Br J Plast Surg. 2004;57:122-33.
- Murray JC, Pollack SV, Pinnell SR. Keloids: a review. J Am Acad Dermatol. 1981;4:461-70.

- Crockett DJ. Regional keloid susceptibility. Br J Plast Surg. 1964:17:245-53.
- Peacock Jr EE, Madden JW, Trier WC. Biologic basis for the treatment of keloids and hypertrophic scars. South Med J. 1970:63:755-60.
- 9. Lee Y, Minn KW, Baek RM, Hong JJ. A new surgical treatment of keloid: keloid core excision. Ann Plast Surg. 2001;46:135-40.
- 10. Kim DY, Kim ES, Eo SR. A surgical approach for earlobe keloid: Keloid fillet flap. Plast Reconstr Surg. 2004;113:1668-74.
- Berman B, Kaufman J. Pilot study of the effect of postoperative imiquimod 5% cream on the recurrence rate of excised keloids. J Am Acad Dermatol. 2002;47(4 Suppl):S209-11.
- Stashower ME. Successful treatment of earlobe keloids with imiquimod after tangential shave excision. Dermatol Surg. 2006;32:380-6.
- Lawrence NT. In search of the optimal treatment of keloids: report of a series and a review of the literature. Ann Plast Surg. 1991;27:164-78.
- Griffith BH, Monroe CW, McKinney P. A follow-up study on the treatment of keloids with triamicinolone acetonide. Plast Reconstr Surg. 1970;46:145-50.
- Shons AR, Press BH. The treatment of earlobe keloids by surgical excision and postoperative triamcinolone injection. Ann Plast Surg. 1983;10:480-2.

- Suliman MT. The keloid fillet flap. Plast Reconstr Surg. 2005:116:337-8.
- Patel PJ, Skinner Jr RB. Experience with keloids after escisión and application of 5% imiquimod cream. Dermatol Surg. 2006;32:462.
- Martín-García RF, Busquets AC. Postsurgical use of imiquimod 5% cream in the prevention of earlobe keloid recurrences: results of an open-label, pilot study. Dermatol Surg. 2005;31: 1394-8.
- 19. Jacobs SE, Berman B, Nassiri M, Vincek V. Topical application of imiquimod 5% cream to keloids alters expression genes associated with apoptosis. Br J Dermatol. 2003;149:62-5.
- Sayah DN, Soo C, Shaw WW, Watson J, Messadi D, Longaker MT, et al. Downregulation of apoptosis-related genes in keloid tissues. J Surg Res. 1999;87:209-16.
- Ladin DA, Hou Z, Patel D, McPhail M, Olson JC, Saed GM, et al. p53 and apoptosis alterations in keloids and keloid fibroblasts. Wound Repair Regen. 1998;6:28-37.
- 22. Berman B, Duncan MR. Short-term keloid treatment in vivo with human interferon alpha-2b results in a selective and persistent normalization of keloidal fibroblast collagen, glycosaminoglycan, and collagenase production in vitro. J Am Acad Dermatol. 1989; 21:694-702.