The combination of suprakeloidal flap and pulsed light heat energy in keloid management: A case report

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ABSTRACT

Yohanes Widodo Wirohadidjojo, Kristiana Etnawati, and Dwi Retno Adiwinarni - The combination of suprakeloidal flap and pulsed light heat energy in keloid management: A case report

The role of chronic tissue hypoxia in the keloid patho-mechanism has been widely accepted. Whereas, the pulsed-light heat energy (LHE) has been developed which has the capacity to generate reactive oxygen species on exposed skin. Although the suprakeloidal flap technique has a high recurrence rate, it was used because of its capacity to prevent suturing hypoxia, thereby the formation of lager recurrent keloid after surgery.

The combination of suprakeloidal flap and pulsed light heat energy was done I the treatment of postvaricella keloid on the right ear lobe of a 9 year old girl. The keloid was excised two times a year ago, but observation one month after the surgery showed a recurrent larger keloid. The performance of suprakeloidal technique followed by pulsed-light heat energy treatment in dose 2.5 J/cm², was administered on day 3rd, day 5th, days 7th, days 9th and day 14th. The flap healed well, attested by the absence of recurrent keloid after forty-five days of observation.

It is concluded that the combination of suprakeloidal flap with pulsed-light energy may be used in keloid management. However, advanced research using better data is needed to reach conclusive evidence.

Key words: keloid - suprakeloidal flap - pulsed-light heat energy - hypoxia

ABSTRAK

Yohanes Widodo Wirohadidjojo, Kristiana Etnawati, and Dwi Retno Adiwinarni - Kombinasi flap suprakeloidal dan pulsed light heat energy pada pengobatan keloid: Laporan kasus

Para ahli sependapat bahwa hipoksia kronis berperan penting pada patofisiologi keloid. Di sisi lain, *pulsed light heat energy* (LHE) merupakan teknik penyinaran yang mampu melepaskan spesies oksigen reaktif dalam jaringan. Para ahli menyarankan operasi flap suprakeloidal pada pengobatan keloid agar hipoksia di tepi jahitan dapat diminimalisasi, sekaligus untuk mencegah keloid kambuhan yang berukuran lebih besar. Seorang anak perempuan berumur 9 tahun menderita keloid paska varisela pada telinga kanan, pernah dioperasi dua kali, keloid kambuh pada bulan pertama pasca-operasi, dan berukuran lebih besar meskipun telah disuntik steroid intralesi. Berdasarkan temuan tersebut, diputuskan pengangkatan keloid dengan teknik flap suprakeloidal diikuti dengan penyinaran LHE sebesar 2,5 J/cm² pada hari ke-3, 5, 7, 9 dan ke-14 pasca-operasi. Hasil tindakan menunjukkan bahwa luka operasi sembuh hamper sempurna dan keloid kambuhan tidak dijumpai meskipun pengamatan telah dilakukan pada hari ke 45.

Disimpulkan gabungan flap suprakeloidal dan terapi menggunakan LHE dapat dikembangkan sebagai salah satu cara pengobatan untuk keloid, meskipun perlu dilakukan penelitian lebih lanjut.

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INTRODUCTION

Various methods have been developed to treat keloid; they include medicinal treatment, such as: triamcinolone, retinoic acid, imiquimod, bleomycine, 5 flourourasil¹, veraprmail^{2,3}, tamoxypen⁴, and several modalities, such as: tumor excision, cryosurgery, LASER, pressure and bandage, silica gel and UVA phototherapy, either in a single modality or in a combined treatment. All of these have unsatisfactory results^{1,5}. The keloid flattening is susceptible to high recurrence rates; post excision recurrences were between 45% to 100%^{1,6}. The recurrent keloids in the aftermath of excision are usually larger than those prior to surgery.

In order to prevent the emergence of larger size keloid after operation, many authors recommend performing various techniques based on intra-keloidal incision such as: W plasty, multiple Z plasty, or M plasty⁷. To prevent the hypoxia caused by skin tension, excessive *undermining* should be performed^{7,8} Adam and Gloster (2002) introduced the suprakeloidal flap technique for treating keloid especially on the ear areas. Based on this technique, skin tension can be avoided and a bigger size recurrent keloid can be prevented⁹.

Pulsed-Light Heat Energy (LHE) is visible light heat energy (400-1200 nm) generated by flash lamp. Atsumi *et al.* (2007) reported the capability of visible light to generate the reactive oxygen species (ROS) of irradiated chromophores¹⁰. These ROS might have the cytotoxic effects as is shown on permanent hair removal effects¹¹ or in the psoriasis treatment¹². The effect of LHE on the prevention of keloid recurrences has never been studied.

CASE REPORT

A nine years old girl was admitted to Dr. Sardjito Dermato-Venereology's Clinic suffering from keloid formation on the right ear, one month after varicella infection. The lesion was excised two times and the aftermath of the above procedures merely led to the formation of recurrent larger keloid. This was the case despite subjecting the patient to several times of intralesional triamcinolone injections following each operation. On undergoing dermatologic examination, the patient was declared healthy but on the upper side of her right ear, a 3x2x1.5 cm3 of keloid with pseudopodia appearance was observed (FIGURE 1). Right in the middle surface of the keloid, a linear sutured scar was also observe, an indication that a simple excision had been performed in the former operation.

After conducting a short discussion, the patient and her mother agreed to the suggestion of undergoing dermatologic surgery, in which the lesion was to be operated using the suprakeloidal flap technique followed by light heat emission therapy.



FIGURE 1. Preoperative Condition

a. Operation techniques

After the measurement of the flap sizes was done and marked basing on the flattened diameter of keloid minus the length of keloid thickness, the area to be operated was disinfected using 10% povidone iodine followed by alcohol 70%. Subsequently, Tumescent local anesthetic was administered, followed by incision of the keloid acme, candidate flap, which was then weakened by semicircular cutting which as made as thin as possible to maintenance nutrition flows. The fibrous material, the depth of adipose tissue on the keloid fringe contraaterally against the flap base was then excised and removed. The attachment of the flap was performed using 6.0 nylon interrupted sutures (FIGURE 2).

b. LHE treatment

The 2.5 J/cm² LHE treatment was administered in concurrence with the schedule of changing the bandage on day three, five, seven, nine, and fourteen (3^{rd} , 5^{th} , 7^{th} , 9^{h} , and 14^{th}).

RESULT

On day three (3) after the operation, some bluish and dark clotting was oberseved on the flap edges, but on the day five, hypoxia signs could no longer be seen. On day 14, the sutures were removed and skin flap was taken perfectly, without any signs of infection. Until day 45 after operation, the recurrent keloid was not observed as depicted in the FIGURE 3.



FIGURE 2. Flap Design



FIGURE 3. Post operative Observation

DISCUSSION

The histological appearance of keloid showed that except for fibroblasts hyper proliferations, the heavy collagen bundles and glycosaminoglicans accumulations were observed in fibrous tissue materials. In normal tissue remodeling, collagen degradation occurred because of collagenase activities which are activated by plasminogen activators. On keloid tissues, observed collagenase accumulation showed feeble activity. The feebleness may due to keloid fibroblasts (KFs) producing plasminogen activator inhibitors (PAI) synthesized under the stimulation of vascular endothelial growth factor-VEGF¹³, one of the prominent growth factor synthesized by KFs¹⁴. VEGF itself was synthesized under hypoxia condition through the binding of hypoxia inducible factor (HIF) on VEGF targeted genes. If hypoxia condition was restored, HIF was perhaps released from VEGF genes and VEGF synthesis stopped.

In a study of Atsumi *et al.* (2007), LHE was found to generate ROS¹⁰. The factor underling the healing of the recurrent keloid in this case becomes clear. ROS generated by LHE in combination with suprakeloidal technique, weakened the sutures, preventing VEGF as well as PAI synthesis in the process. This made the remodeling processes to run effectively. In this case, the effect of LHE on the hypoxia condition was observable exactly from day three, to day seven, attested by replacement of the bluish color of the flap with the fresh red color (FIGURE 3).

In vitro study, it became evident that keloid fibroblasts produced more noticeable type I procollagen than normal fibroblasts (NFs). Previous studies indicated that type III procollagen didn't replace this procollagen as shown among NFs. Lubart *et al.* (2007) study, found that visible light might stimulate fibroblast to synthesize new collagen especially type III procollagen¹⁵. LHE induced new type of collagen synthesis may serve as another explanation of the no recurrent keloid in this case, even though similar findings have ever been reported among KFs.

A number of studies showed that KFs was resistant to Fas induced apoptosis¹⁶ and ceramide stimulation, due to an increase of insulin like growth factor receptor expression¹⁷. The alteration of KFs might induce KKs to stimulate KFs to produce Bcl-2, ERK, and IP3, which have anti-apoptotic effects¹⁸. Although visible light penetration is limited on the epidermal surface, the visible light may stimulate of epidermal keratinocytes apoptosis as shown by Lascaratos et al. (2007) on rat retinal cells¹⁹. The death of KKs may affect KFs resistance to apoptosis, and as a result, KFs proliferation may be inhibited and new keloid formation can be prevented.

Based on the above explanation, together with a successful treatment of a single case of keloid, a conclusion is drawn that a combination of suprakeloidal technique together and LHE treatment can be used to treat keloid. However, more research on the subject is needed.

REFERENCES

- 1. Olabanji JK, Onayemi O, Olasode GA, Lawal OAR. Keloids: An old problem still searching for a solution. Surgical Practice, 2005; 9:2-7.
- G. Giugliano, D. Pasquali, A. Notaro, S. Brongo, G. Nicoletti, F. D'Andrea, A. Bellastella, A. A. Sinisi. Verapamil inhibits interleukin-6 and vascular endothelial growth factor production in primary cultures of keloid fibroblasts. Br J Plast Surg. 2003; 56(8): 804-9.
- Copcu E, Sivrioglu N, Oztan Y. Combination of surgery and intralesional verapamil injection in the treatment of the keloid. J Burn Care Rehabil. 2004; 25(1): 1-7.
- 4. Mikulec AA, Hanasono MM, Lum J, Kadleck JM, Kita M, Koch RJ. Effect of tamoxifen on transforming growth factor beta 1 production by keloid and fetal fibroblasts. Arch Facial Plast Surg. 2001; 3(2): 111-14.
- Marneros AG, and Krieg T. Keloid-clinical diagnosis, pathogenesis, and treatment option. JDDG. 2004; 11: 905-13.
- Chowdri NA, Mattoo MMA, and Darzi MA. Keloids and hypertrophic scars: results with intra-operative and serial postoperative corticosteroid injection therapy. Aust. N.Z.J. Surg. 1999; 69: 655-59.
- Decherd MD, Calhoun KA, Quinn FB, Ryan MW. Scar revision and camoflouge. Postgraduate Training Program of the UTMB Department of Otolaryngology/Heat and Neck Surgery, April 24, 2002.
- Kelly P. Medical and surgical therapies for keloids. Dermatol Ther. 2004; 17: 212-18.
- Adam BB and Gloster HM. Surgical pearl: excision with suprakeloidal flap and radiation therapy for keloids. Am J. Dermatol. 2002; 47: 307-9.
- Atsumi T, Tonosaki K, Fujisawa S. Comparative cytotoxicity and ROS generation by curcumin and tetrahydrocurcumin following visible-light or treatment with horseradish peroxidase. Anticncer Res. 2007; 27(1A): 363-7.

- 11. Sadick NS, Krespi Y. Hair removal for Fitspatrick skin tpes V and VI using light and heat energy technology. J Drugs Dermatol. 2006; 5(8): 724-26.
- 12. Leviav A, Wolf R, Vilan A. Treatment of psoriasis with light and heat energy (LHE): A preliminary study. Dermatol Online J. 2004; 15; 10(2): 4.
- Wu Y, Zhang Q, Ann DK, Akhondzadeh A, Duong HS, Messadi DV, Le AD. Increased vascular endothelial growth factor may account for an elevated level of plasminogen activator inhibitor-1 via activating ERK1/ 2 in keloid fibroblasts. Am J Physiol Cell Physiol. 2003; 26: 1123-28.
- 14. Fujiwara M, Muragaki Y, Ooshima A. Upregulation of transforming growth factor-beta1 and vascular endothelial growth factor in cultured keloid fibroblasts: relevance to angiogenic activity. Arch Dermatol Res. 2005; 297(4): 161-69.
- 15. Lubart R, Friedmann H, Lavie R, Longo L, Jacobi J. A reasonable mechanism for visible light-induced skin rejuvenation. Lasers Med Sci. 2007; 22(1): 1-3.

- 16. Chodon T, Sugihara T, Igawa HH, Funayama E, Furukawa H. Keloid derived fibroblasts are refractory to Fas mediated apoptosis and neutralizing TGF betha can abrogate this resistance. Am. J. Pathol. 2000; 157: 1661-69.
- Ishihara H, Yoshimoto H, Fujioka M, Murakami R, Hirano A. Keloid fibroblasts resist ceramide induced apoptosis by over expression IGF1 receptors. J. Invest Dermatol. 2000; 115: 1065-71.
- Funayama E, Chodon T, Oyama A, Sugihara T. Keratinocytes promote proliferation and inhibit apoptosis of underlying fibrolasts: An important role in pathogenesis of keloid. J Invest Dermatol. 2003; 121: 1326-31.
- 19. Lascaratos G, Ji D, Wood JP, Osborne NN. Visible light affects mitochondrial function and induces neuronal death in retinal cell cultures. Vision Res. 2007 Feb 15; [abstr., Epub ahead of print.