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Case Report

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Combination of Fractional Er:YAG Laser, Pulsed Dye Laser, and Intralesional Triamcinolone With 5-Fluorouracil for Keloid Treatment

Bonnie Yudistha Anggawirya[1], Putri Hendria Wardhani[1], Diah Mira Indramaya[1], Muhammad Yulianto Listiawan[1*]

[1]Department of Dermatology and Venereology, Faculty of Medicine, Airlangga University, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

***Correspondence to**
Muhammad Yulianto Listiawan;
Email: m.yulianto@fk.unair.ac.id

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Abstract

Introduction: Benign fibroproliferative scars that are larger than the initial lesion are called keloids. Keloids treatment in clinical practice is still difficult. Although there are various therapy choices, none is embraced by everyone or is relapse-free. Various treatment modalities such as intralesional corticosteroid injection with 5-fluorouracil (5-FU), fractional Er:YAG laser, pulsed dye laser (PDL), and others can be used either as monotherapies or combined therapies. Therefore, efforts should be made to select the treatment that will provide the best results.

Case Presentation: A 6-year-old boy with keloids on the lower lips extending to the chin was successfully treated with a 2940-nm fractional Er:YAG laser alternated with a 595-nm long-PDL followed by the combined intralesional injection of corticosteroid and 5-FU. The patient was followed up for 1 year with no lesion recurrence.

Conclusion: Our case supports a combined therapy to successfully treat a patient with a keloid on the chin. Therapy using a combination of these four modalities seems safe and effective and may have a synergistic effect with minimal downtime.

Keywords: 5-Fluorouracil; Er:YAG laser; Intralesional; Keloid; Pulsed dye laser.

Introduction

Excessive scarring is ugly and typically causes people afflicted to experience emotional stress.[1] The need for therapy is obvious, and it is not based on only cosmetic factors since pruritus, contractures, and discomfort often accompany it.[2] Dermal connective tissue benign hyperproliferations are known as keloids. Injuries to the deep dermis often lead to the production of scar tissue.[3] Keloids are scars that extend beyond the boundaries of the initial injury and do not regress, in contrast to normal and hypertrophic scarring. Following disruption of skin integrity brought on by both superficial and deep traumas, keloids may develop within months to years. The precise pathophysiology of keloid development has not yet been clarified because of the intricacy and mechanical factors at play throughout the wound-healing process. Keloid risk factors include ethnic groups with darker skin, pregnancy, puberty, skin injury on osteogenic surfaces, and personal or family history of the condition.[4] According to reports, 4.5% to 16% of those with darker skin will develop keloids.[5]

There are many treatment options available for the treatment of keloids, with varying degrees of success based on time to relapse.[4] An efficient treatment regimen is essential since keloids are frequent and they often return. There is no consensus on ideal standard therapy.[5] The treatment methods used to address severe scarring have considerably improved over time. The first course of keloid treatment is an intralesional triamcinolone injection (TAC).[1] When combined with 5-fluorouracil (5-FU), these agents are more effective and safer. Many laser methods have recently been established as beneficial parts of the total therapy approach utilized to treat keloids. Both the non-ablative pulsed dye laser (PDL) and the ablative fractional Er:YAG laser have shown encouraging outcomes and are regarded as effective therapy techniques.[6]

Case Report

A 6-year-old boy presented with a 1-year history of keloids on both ends of the lower lip extending to the chin with a history of burn scar. The patient was treated with intralesional TAC (10 mg/mL) at 0.05-0.1 mL/cm^2 at 4-week intervals for only 2 times with little thinning of the lesions noted (Figure 1A). However, the patient's parents were seeking a better treatment due to the pain of the injection. Surgical excision and laser therapy were discussed as treatment options. A combination of

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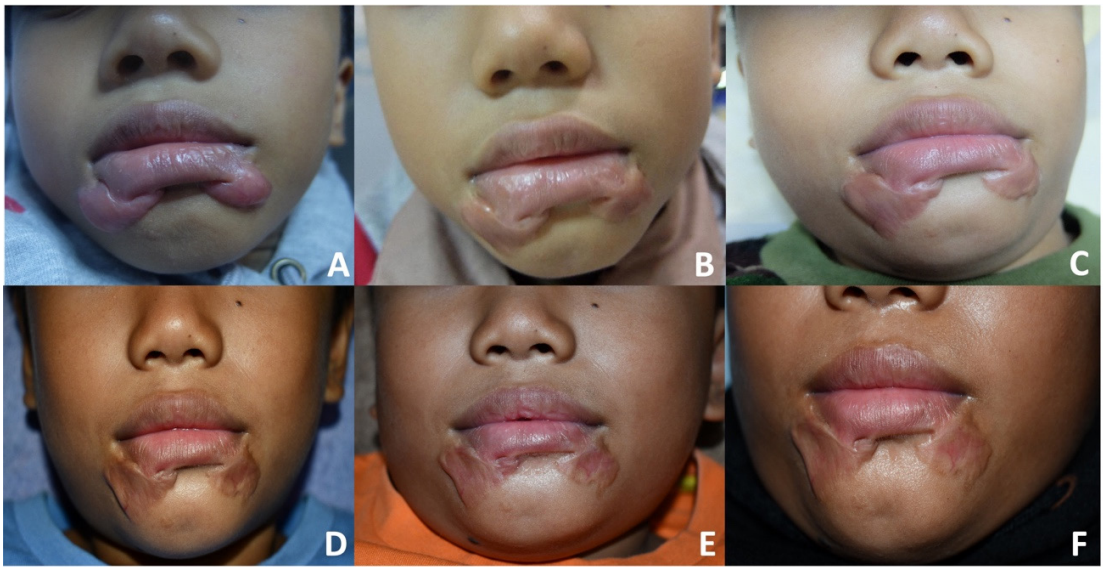

Figure 1. (A) Keloids on both ends of lower lips extending to the chin prior to combination treatment; (B-E) Appearance at follow-up: noticeable progression of the thinning of keloids; (F) Keloids decreased significantly after combination treatment, but telangiectasia is still visible

TAC + 5-FU and laser was the treatment of choice for a better outcome. The patient was then referred to our satellite clinic (Surabaya Skin Centre – Laser Medicine Clinic) for further treatment.

Before the treatment, a 1-hour-long topical application of 5% lidocaine cream was made to the treatment region under occlusion. A fractional Er:YAG laser at 2940 nm and a long-pulsed dye laser at 595 nm were both used on the subject. After each laser therapy session, the patient had intralesional injections of TAC 40 mg/mL and 5-FU 50 mg/mL in a 1:1 ratio at 0.05-0.1 mL/cm^2. The patient was advised to apply antibiotic ointment after each session for 7 days. A total of 7 sessions of fractional Er:YAG laser and 8 sessions of PDL laser treatment were performed over a 3-year period. The fractional Er:YAG laser (2940 nm) treatment settings were 10-20 W, 800 µs pulse duration, 3 stacks per shot, with 15-17 m J/cm^2 fluence. The PDL (585 nm) treatment parameters were fluence of 5.25-8.50 J/cm^2, a spot size of 7–10 mm, a pulse length of 3–10 ms, and 20 pulses per treatment. The patient and the medical professional caring for them continued to perceive gains after each treatment session. A year of patient monitoring revealed no recurrence of the lesion.

Discussion

There are several treatment plans for keloids, and treating them might be difficult. No widely approved therapy plan can completely and permanently resolve these issues, and various treatment regimens have been utilized with varying degrees of effectiveness.[7] At the locations of past dermal damage and wound healing, excessive collagen is deposited and causes keloids. Although the precise pathophysiology of scarring is uncertain, new research points to the significance of the transforming growth factor-β (TGF-β) family of proteins in cutaneous scarring. Fibrosis and severe scar tissue deposition may result from excessive TGF-β overproduction. Abnormally high levels of IL-6, IL-13, and IL-15 may also play a role in keloid development.[8]

There are several therapeutic options for keloids at the moment, including laser therapy, radiation therapy, intralesional steroid injection, intralesional 5-FU injection, surgical excision, and the use of silicone gel sheets.[4] Success rates are said to vary. Recurrence is commonly seen even with combined treatment.[9] However, which of the available therapy techniques may be considered the optimal treatment choice has been challenging to evaluate owing to the absence of high-quality, controlled comparison studies. Intralesional corticosteroid injection is one of the mainstays of keloid therapy; however, its effectiveness is not entirely satisfying.[4,5] By reducing inflammation during the healing phase of a lesion, corticosteroids impact several crucial pathways in treating keloids.[10] Intralesional TAC injection is associated with inhibiting fibroblast proliferation, TGF-β, and suppressing collagen production via lower gene expression in keloids.[5]

For many months or until the scar is flattened, the dose and the treatment interval have been adjusted to range from 10 to 40 mg/mL given every 4-6 weeks.[4] Although intralesional TAC treatment has shown 50%–100% clinical effectiveness, the outcomes have been ambiguous and linked to several unfavorable side effects, including atrophy, telangiectasia, and pigmentary alterations, which most patients do not accept.[11]

A pyrimidine analog known as 5-FU has been proven to have a relatively quicker reaction in terms of scar flattening. TAC and 5-FU together may result in a quick response for scar flattening with the additional benefit of fewer side effects.[12] 5-FU is an antimetabolite

that also suppresses fibroblast proliferation and TGF-β-induced type I collagen gene production.[6] Keloids and hypertrophic scars may be treated with intralesional 5-FU delivery once every two weeks or once a week.[11]

5-FU injections have typically been combined with a corticosteroid to reduce the adverse effect of erythema.[13] It alleviates discomfort, stinging, swelling, purpura, and hyperpigmentation at the injection site.[14] Fitzpatrick was the first to share their TAC + 5-FU experience. Fitzpatrick's regimen increased effectiveness, and injections were less unpleasant (a 9:1 ratio of 5-FU to steroid was employed). Fitzpatrick said that while the low dosage of triamcinolone has no extra therapeutic benefit, it lessens the possibility of erythema as a side effect of 5-FU injection alone.[15] Davison et al. presented their findings on 102 keloids, showing that patients who had excision followed by the 5-FU/steroid combination had 92% effectiveness, compared to those who did not get 5-FU, with 73% efficacy.[5] Forty keloids were treated by Darougheh et al either with TAC alone or with TAC plus 5-FU. It shows that the TAC + 5-FU combination is more efficient and offers a quicker response with fewer adverse effects than the TAC group.[11]

Ablative laser systems and PDLs, which encourage the repair of pathologic scars by stimulating collagen remodeling, lowering cellular activity via laser-induced tissue hypoxia, and decreasing the synthesis of TGF-β1, were the main focus of earlier research detailing laser therapies for keloids.[16] Ablative lasers, such as the 2940-nm erbium-doped: yttrium, aluminum garnet (Er:YAG) laser, produce beams that are absorbed by skin water and cause localized tissue damage. The Er:YAG laser is more accurate and has a stronger affinity for water for treating elevated scar margins.[17] Ekstein et al evaluated the effectiveness of light-, laser-, and energy-based therapies for keloid scars. Eight months after receiving Er:YAG laser treatment, there was a 22% recurrence rate.[4] One clinical trial that assessed the effectiveness of Er:YAG in treating keloid scars has been published. Up until scar flattening was accomplished, a combination therapy using the Er:YAG laser and twice-daily topical betamethasone under occlusion was performed.[18]

The 585-nm PDL has recently gained popularity as a keloid therapy method, either alone or in conjunction with other treatments such as topical 5-FU and TAC.[19] The PDL treatment works by specifically harming the keloid's microvasculature.[5,7] PDL treatment normalizes the surface of the wound, smooths out the texture, helps the scar fit in with the surrounding skin, and reduces erythema.[5] TGF-β1 levels have risen in particular in vitro studies of keloidal fibroblasts exposed to low-fluence PDL (3 J/cm^2), as in up-regulation of other factors that promote collagen production. This effect was not seen at a slightly higher fluence.[19]

We selected targeted, multimodal, minimally invasive therapies for this patient, focusing on normalizing dermal thickness and improving color and texture. Although further studies are needed to confirm this finding, we propose that a combination of these four modalities may have a synergistic effect and induce a more rapid and robust treatment response with minimal adverse effects or downtime.

Conclusion

Following a combined treatment plan for our patient, we saw improvements in both appearance and functionality. Our patient showed dramatic improvements with the combination of several proven treatment modalities. In this case, the combination of TAC + 5-FU with Er:YAG laser and PDL had a synergistic effect with impressive results. This is the first time both modalities have been combined. Future research on this combination therapy may confirm our current combo strategy.

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Authors' Contribution

Conceptualization: Bonnie Yudistha Anggawirya.
Funding acquisition: Bonnie Yudistha Anggawirya.
Investigation: Putri Hendria Wardhani.
Supervision: Muhammad Yulianto Listiawan.
Validation: Diah Mira Indramaya.
Visualization: Bonnie Yudistha Anggawirya, Putri Hendria Wardhani, Indramaya DM, Muhammad Yulianto Listiawan.
Writing–original draft: Bonnie Yudistha Anggawirya.
Writing–review & editing: Bonnie Yudistha Anggawirya, Putri Hendria Wardhani.

Competing Interests

The authors declared no potential conflicts of interest.

Informed Consent

The authors confirm that the necessary written, informed consent was obtained from the patient's parent for this article.

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