e-ISSN: 2747-2051

Archives of the Medicine and Case Reports

[AMCR]

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# Comparison of Intralesional Triamcinolone Acetonide Alone with Intralesional Triamcinolone Acetonide-5-Fluorouracil Combination Injection in Keloid: A Case Report

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**ARTICLE INFO**

**Keywords:**
5-FU
Fluorouracil
Keloids
Scar
Triamcinolone acetonide

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All authors have reviewed and approved the final version of the manuscript.

*https://doi.org/10.37275/amcr.v5i3.565*

**A B S T R A C T**

Keloids are abnormal cutaneous wound healing responses extending beyond the borders of the initial wound, usually appearing pink-purplish to hyperpigmented nodules or plaques with a hard consistency, irregular shape, uneven border, and smooth shiny surface. Most often occur on the chest, shoulder, upper arms, earlobes, and cheeks. This case report aims to compare a case of keloid treated with intralesional triamcinolone acetonide (TAC) alone with intralesional triamcinolone acetonide-5-fluorouracil (TAC + 5-FU) combination injection. A 21-year-old Minahasa male complains of growing pruritic scars in the back area and right and left upper arms since five years ago. Physical examination of the right and left upper arms revealed multiple hyperpigmented nodules and plaques, irregularly shaped, smooth, and shiny surfaces with defined borders and varying sizes. A clinical diagnosis of keloid was made. Treatment was initiated with weekly intralesional TAC alone on the left upper arm vs. intralesional TAC + 5-FU combination injection on the right upper arm. The evaluation was made based on the clinical and modified Vancouver scar scale. One of the most commonly used therapeutic options for keloid is TAC. However, the combination of TAC + 5-FU may be opted for due to its mechanism through the corticosteroid mechanism of action in conjunction with the antimetabolite activity of 5-FU. The combination may yield a more effective and faster outcome with fewer side effects. Intralesional combination TAC + 5-FU injection may be a therapeutic option for keloid with minimal side effects.

## 1. Introduction

Keloids are abnormal cutaneous wound healing responses characterized by the growth of excessive localized scars as a response to cutaneous trauma, burn, or infection.[1,2] Most people who experienced keloids are young adults aged 10-30 years and were reported to occur in 5-15% of all wounds.[2] The etiology of keloid is unclear, yet genetic factors increase the incidence of keloid.[3] Keloids more commonly affect African, Asian, and Hispanic descent.[4] Women have a greater predisposition in some ethnic groups.[1]

Keloids form several weeks to months after the initial lesion and grow beyond the lesion boundaries. The initial clinical picture of keloids is pink-purplish to hyperpigmented nodules or plaques with a hard consistency, irregular shape, uneven border, and smooth shiny surface. Telangiectasia may be noted. Subjective complaints of pruritus or pain may be reported.[1,5] Over time, keloids may soften.

Keloids may occur on all body parts but are most commonly reported in the chest, shoulder, upper arms, earlobes, and cheek regions.[5] Differential diagnosis of keloids includes hypertrophic scars and dermatofibrosarcoma protuberans.[1]

Keloids have many therapeutic options, including intralesional corticosteroid injections, 5-fluorouracil injections, surgical excision, radiotherapy, silicone gel, laser, and combination therapy, to name a few. There is no gold standard for keloid therapy.[2,6] This case report will compare intralesional triamcinolone acetonide (TAC) injection alone with intralesional TAC and 5-fluorouracil (5-FU) combination in a keloid patient. This case is reported according to the CARE guidelines.[7]

## 2. Case Presentation

A 21-year-old Minahasa male presented to the outpatient department with growing pruritic scars in the back area and right and left upper arms since five years ago. The patient denied pain or a history of bleeding from the lesions. Past history revealed numerous treated inflammatory acne; however, the acne resolved with extensive scars. Past medication history for other systemic diseases was denied. In the family, the patient's mother also experienced a similar condition of acne, acne scars, and keloids. On physical examination (week 0), the right and left upper arms revealed multiple hyperpigmented nodules and plaques, irregularly shaped, smooth, and shiny surfaces, with defined borders, and varying sizes of the following (Table 1, Table 2, and Figure 1). The complete blood count was within normal limits. A diagnosis of keloid was established, and the patient was planned for a weekly intralesional TAC and 5-FU injection for ten weeks.

To evaluate and compare the effectiveness of intralesional TAC alone vs. intralesional TAC + 5-FU combination injection; intralesional TAC alone injections were performed on the left upper arm, while the combination injection of TAC + 5-FU was performed on the right upper arm. The injections were carried out weekly until the tenth week. Evaluation of keloid was carried out using the modified Vancouver scar scale (VSS). The intralesional injection dose for the TAC alone and TAC + 5-FU (ratio of 1 TAC-to-9 5-FU) combination were 0.1–0.2 cc per lesion. Lesions were treated with 2% fusidic acid post-injection.

The effectiveness (>50% reduction in initial scar height) was superior for the combination injection of TAC+ 5-FU than that of the intralesional TAC alone injection. In the tenth week, three lesions on the combination injection arm lost 100% of their height compared to a 50% reduction in the TAC alone injection. A noted side effect was pain on the injection side for a few hours after the injection for combination therapy of TAC + 5-FU's side.

## 3. Discussion

The diagnosis of this case was based on the history taking and physical examination. Keloids are hyperproliferative growth constituting type III collagen at the initial phase or type I collagen at the final phase.[8] In addition to the initial cutaneous trauma (e.g., burn, sharp injury, operation scar, acne, and/or insect bite), psychological stress has been hypothesized as a risk factor for keloid growth due to the stress hormone.[9] Differential diagnoses of keloid include hypertrophic scar and dermatofibrosarcoma protuberans (DFSP).[6] Hypertrophic scar is characterized by a heightened or thickened scar

occurring after trauma or inflammation with growth within the initial insult and may regress after a few months to years. DFSP is a malignant soft tissue tumor that grows slowly and often occurs in adults. DFSP appeared as a painless reddish-purple plaque that grows gradually. Untreated DFSP lesions usually develop into nodules or tumors that may ulcerate and bleed.[1,6] Keloids differ from hypertrophic scars due to the growth of scar extending over the initial trauma and tend to be stable without any tendency for regression.[1] In this case, the scar grew over the border of the initial trauma and was evolving.

This case compared intralesional treatment of TAC + 5-FU combination injection on keloid lesions on the right arm and intralesional TAC alone injection on the left arm. The maximum dose of the combination injection was 0.2 cc of 40 mg/mL TAC and 1.8 cc of 50 mg/mL 5-FU. The superiority of the combination injection was the pain reduction during injection.[4, 6] The small amount of TAC used in combination with 5-FU is not therapeutic, but it might play an essential role in reducing 5-FU-induced inflammation.[10] The mechanism of TAC is achieved through its property as a long-acting corticosteroid, i.e., inhibiting the migration of inflammatory cells, inhibiting the proliferation of fibroblast during wound healing, inhibiting collagen synthesis, increasing collagenase production, and reducing collagenase inhibitor concentration. The dose for intralesional TAC is 10–40 mg/mL injected at a one-week interval for each session.[8]

5-fluorouracil is a pyrimidine analogue with antimetabolite activity that interferes with ribonucleic acid (RNA) synthesis and inhibits fibroblast proliferation, reducing scar tissue creation. Intralesional 5-FU can be used as a monotherapy or in combination with TAC.[1, 8] The dose of 5-FU given as a monotherapy in keloids can vary between 50–150 mg with a varying treatment duration between one to 16 sessions before showing improvement in keloid lesions, with an interval of one to two weeks per session.[1] Intralesions 5-FU injection (50 mg/mL) is given at 0.05 mL/cm or until a pale-whitish area is observed.[4] As the keloid scar is in a hypermetabolic state, the use of antimetabolite as a treatment option is logical. The hyperactive fibroblasts lay down excessive collagen. Regression of these fibroblasts is dose and time-dependent.[11] This rationalizes the use of 5-FU as an antimetabolite drug for keloid. Additionally, this was further supported histopathologically by a study comparing the efficacy and safety of intralesional TAC versus 5-FU versus a combination of TAC + 5-FU, reporting a significantly reduced Ki-67 proliferative index after treatment with 5-FU (P value 0.001) and combination of TAC + 5-FU (P value 0.003).[12]

Several studies have compared the effectiveness between TAC alone injection and TAC + 5-FU combination injection in keloid and concluded that both were effective in the treatment of keloid; yet, the combination therapy of TAC + 5-FU was more effective and faster with fewer side effects.[8,12] This study revealed a higher efficacy in the combination therapy of TAC + 5-FU than the TAC alone injection, where a striking reduction in lesion height was noted. This finding is in line with other studies.[13-15] The most frequent side effects associated with TAC injection are telangiectasia, atrophy, pain, and pigmentation changes, and rare systemic side effects of Cushing syndrome may occur. The side effects of 5-FU are pain, purpura at the injection site, ulceration, hyperpigmentation, a burning sensation at the injection area, and ulceration. Systemic toxicity, linked to intravenous use, of 5-FU may depress bone marrow function and cause gastrointestinal disturbance (vomiting or diarrhea).[1,8,16,17] In this case, the patient did not experience significant side effects, except for pain at the injection side for a few hours after injection for combination therapy of TAC + 5-FU's side similar to other studies.[17,18]

Other different therapeutic modalities for keloid may include surgical excision, topical silicone gel

sheeting, onion extract gel, enzyme (collagenase and hyaluronidase) laser therapy, cryotherapy, photodynamic therapy, anti-hypertensive pharmaceuticals, botulinum toxin A, calcineurin inhibitors, doxorubicin, electrical stimulation, microneedling physical contact, extracorporeal shockwave therapy, fat grafting, stem cell therapy, imidazoquinolines, platelet-rich plasma, interferons, tamoxifen, RNA-based therapies, each with varying strength of recommendations and level of evidence. However, a more effective therapeutic regimen has yet to be pointed out as the gold standard. Given the complex process of keloid formation, a deeper understanding of the molecular mechanisms driving keloids' development and recurrence would cater to innovative treatments' development.[19-22]

This case utilized the modified VSS to evaluate the keloid pre- and post-injection. According to the literature, VSS is the first widely used validated scar scale in clinical practice to assess burn scars and remains one of the most frequently used today. This scale focuses on four objective parameters: scar height/ thickness, flexibility, vascularization, and pigmentation. In this case, VSS is implemented: keloid height is measured with a ruler or caliper, elasticity is assessed by palpation, vascularity is evaluated by visual inspection, and pigmentation is assessed after blanching and compared with the surrounding skin.[1] However, the VSS has its limitations. Hence, the modified VSS was developed. The modified VSS introduced two additional subjective parameters: pain and itching.[23] The patient's modified VSS were 11-12 and 7-8, pre- and post-injection, respectively. The prognosis of this case is good, yet recurrency still needs to be exempted. The keloid recurrence rate can be up to 50%, but the risk factors that influence the recurrence are unknown.[1]

Table 1. Size and modified Vancouver scar scale of the keloid on the right upper arm.

| | **Week 0** | | **Week 5** | | **Week 10** | |
|---|---|---|---|---|---|---|
| **Lesion number** | **Size (length x width x height)** | **Modified VSS** | **Size (length x width x height)** | **Modified VSS** | **Size (length x width)** | **Modified VSS** |
| 1 | 2,5 x 1,5 x 0,2 cm | 12 | 2,5 x 1,5 x 0,1 cm | 11 | 2,5 x 1,5 cm | 7 |
| 2 | 3,3 x 1,8 x 0,2 cm | 12 | 3,3 x 1,8 x 0,1 cm | 11 | 3,3 x 1,8 cm | 7 |
| 3 | 2,1 x 1 x 0,1 cm | 11 | 2,1 x 1 cm | 10 | 2,1 x 1 cm | 7 |

VSS = Vancouver scar scale.

Table 2. Size and modified Vancouver scar scale of the keloid on the left upper arm.

| | **Week 0** | | **Week 5** | | **Week 10** | |
|---|---|---|---|---|---|---|
| **Lesion number** | **Size (length x width x height)** | **Modified VSS** | **Size (length x width x height)** | **Modified VSS** | **Size (length x width x height)** | **Modified VSS** |
| 1 | 3,5 x 1,5 x 0,2 cm | 12 | 3,5 x 1,5 x 0,2 cm | 11 | 3,5 x 1,5 x 0,1 cm | 7 |

VSS = Vancouver scar scale.

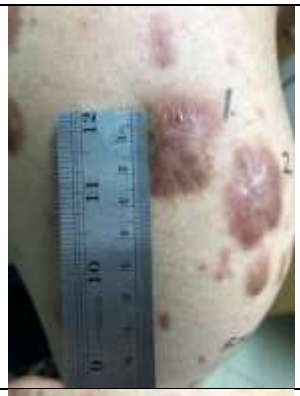
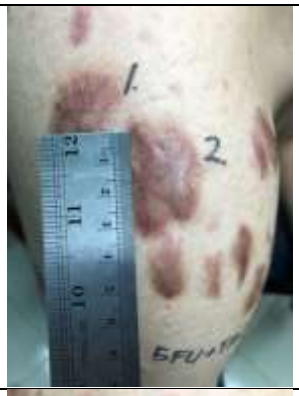
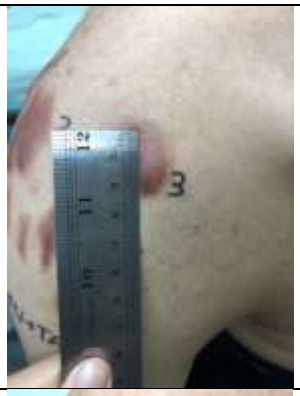
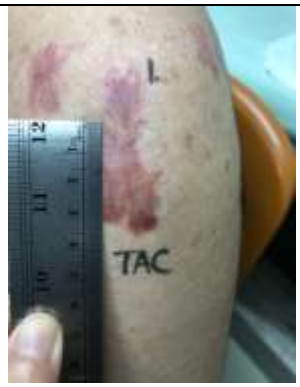
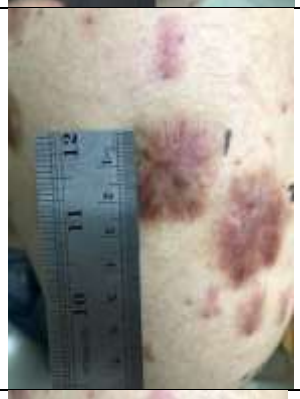
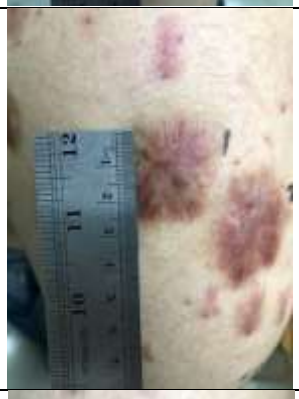
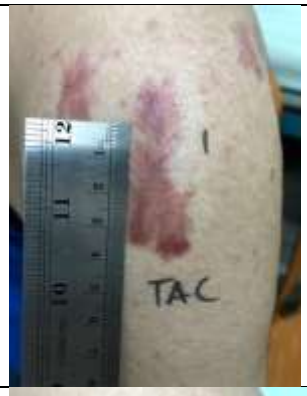
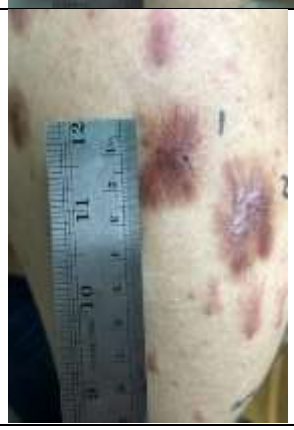
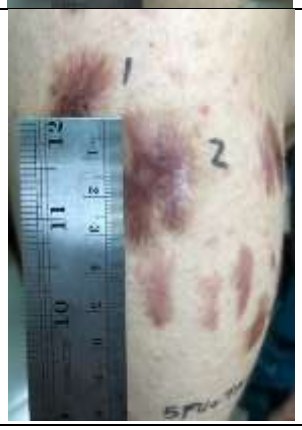
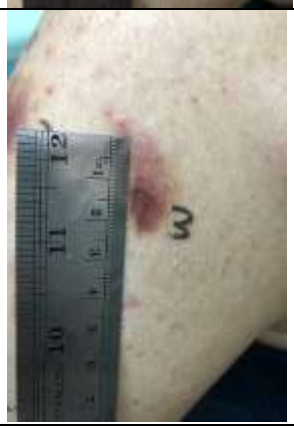
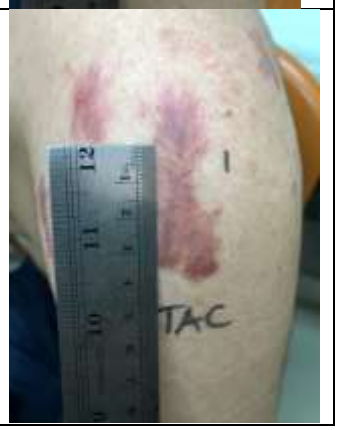
| | Right upper arm lesion | | | Left upper arm lesion |
|---|---|---|---|---|
| **Week number** | Lesion 1 | Lesion 2 | Lesion 3 | Lesion 1 |
| Week 0 |  |  |  |  |
| Week 5 |  |  |  |  |
| Week 10 |  |  |  |  |

Figure 1. Evolution of right and left upper arm lesions throughout the injection.

## 4. Conclusion

This case report highlighted the comparison between intralesional TAC alone and the intralesional combination of TAC + 5-FU in keloid. The diagnosis of keloid was made from history taking and physical examination. Both options effectively treated keloids, yet the intralesional combination of TAC + 5-FU was favorable with minimal side effects.

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