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Combination of triamcinolone/5FU with multiple Z-plasty: A powerful duo to combat cicatricial ectropion

Andi Pratiwi, Halimah Pagarra, Suliati Amir, Junely Vimala Jaury, Syukriah Sofyan, Sisca Sisca

ABSTRACT

Introduction: Cicatricial ectropion, a condition characterized by eyelid malposition and conjunctival exposure, can result from trauma, scarring, or surgical interventions. Management requires a personalized approach, as various treatments show limited success when used alone.

Case Report: A 43-year-old patient presented with severe cicatricial ectropion. Examination showed significant keloid traction along the upper and lower eyelid margin and an extensive hypertrophic scar extending from the lower eyelid to the cheek. A combination of intralesional injections of 5-fluorouracil (5-FU) triamcinolone acetonide (TA) was administered in four cycles. This was followed by surgical correction using multiple Z-plasty on the lower eyelid. Postoperatively, no ectropion remained, and favorable results were noted six months later with no significant side effects.

Conclusion: The combination of 5-FU and TA, followed by Z-plasty, provides an effective and promising approach for treating severe cicatricial ectropion. This method improves scar reduction and skin pliability, offering functional and aesthetic benefits with minimal complications compared to traditional treatments like skin grafting.

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INTRODUCTION

Cicatricial ectropion is characterized by the shortening and presence of a vertical anterior lamella scar, often attributed to chemical or thermal trauma, postoperative scarring, chronic inflammation, and involutional changes. Managing ectropion remains a challenge for surgeons, requiring an individualistic method. The selection of surgical procedures should be guided by a thorough preoperative examination, considering both the etiology and anatomical location [1].

Numerous pharmacological agents have been investigated for effectiveness as monotherapy or in combination with ectropion management. These include surgical excision, topical and intralesional steroids, cryosurgery, radiation therapy, laser treatment, and several others, but no single method offers comprehensive benefits. Medical management remains complex due to diverse efficacy, potential side effects, and high probability of recurrence [2].

The existing literature offered many treatment possibilities, but all lacked definitive proof of effectiveness. Despite the continuous evolution of surgical methods, the role of antimetabolites [5-fluorouracil (5-FU)] and anti-

inflammatory (TA) agents in addressing the biological processes of wound healing and scar formation has been widely recommended as definite and necessary. Intralesional injection of these drugs followed by surgical excision had been successful in terms of reducing size, improving vascularity, and enhancing skin pliability while offering faster and more efficacious results with fewer unwanted side effects in the reported case [3–5].

We presented the therapeutic outcomes of a patient with an extensive hypertrophic scar and severe cicatricial ectropion in this case report. The treatment comprised a combination of 5-FU and triamcinolone 10%, followed by eyelid reconstruction surgery using multiple Z-plasty methods which produced a satisfactory outcome. Available information shows that reports in the literature on the combination of regimens used prior to surgical management of severe cicatricial ectropion are limited.

CASE REPORT

This manuscript is a single-patient case report. The patient was a 43-year-old man who presented with imperfect closure of the right eyelid for one month after prior lower eyelid repair and facial reconstruction performed at another center. His recent symptoms included redness and excessive tearing of the affected eye. On examination, the right eye showed a phthisical globe with no light perception, significant keloid traction of the upper eyelid margin, and an extensive hypertrophic scar involving the lower eyelid and extending to the cheek, producing severe cicatricial ectropion. Associated findings included conjunctival exposure/chemosis, corneal scarring, and leukoma, whereas the left eye was within normal limits.

Treatment consisted of serial intralesional injections followed by reconstructive surgery. A mixture of 0.3 mL of 5-FU (15 mg 5-FU) and 0.1 mL of triamcinolone acetonide (TA) (1 mg TA) was administered intralesionally in both the superior and inferior palpebra without local infiltration of anesthetic. The injections were administered intradermally using a 27G insulin syringe, with 0.1 mL per site placed approximately 1 cm apart throughout the lesion with a maximum of 2 mL per session. The needle was inserted at a 15-to-30-degree angle directly into the mid-to-deep dermis and superficial subcutaneous layer of the hypertrophic scar tissue, avoiding deeper orbital structures or direct infiltration into the orbicularis oculi muscle. The treatment course was planned as serial monthly injections with reassessment at each visit. The four-week interval was based on published intralesional 5-FU/triamcinolone protocols and the expected duration of antifibrotic activity. Treatment cycles were determined by clinical response, particularly reductions in scar height and induration, improved tissue pliability, and the absence of limiting adverse effects. Serial clinical examination and interval photographs demonstrated progressive flattening of the hypertrophic scar and softening of the periocular tissues over the four treatment sessions. Although no formal scar scale or quantitative lid tension measurement was performed, these clinical changes suggested improved local tissue compliance before surgery (Figure 1).

Following this response, the patient underwent multiple Z-plasty of the lower eyelid under general anesthesia. The procedure involved incision along the scar, excision of subcutaneous fibrotic tissue, and creation of multiple 60-degree incisions from each end of the excised scar to raise skin flaps. These flaps were undermined and rotated upward and downward to create reversed Z configurations, then secured with 6-0 nylon sutures to release tension along the inferior lid margin and anterior lamella. Postoperatively, the lower lid ectropion resolved, and the wound healed in less than one month. At six months of follow-up, the cosmetic outcome was described as favorable, with no skin depigmentation or telangiectasia, although a minimal area of cheek atrophy remained (Figure 2). Further corrective treatment for the upper lid ectropion was planned.

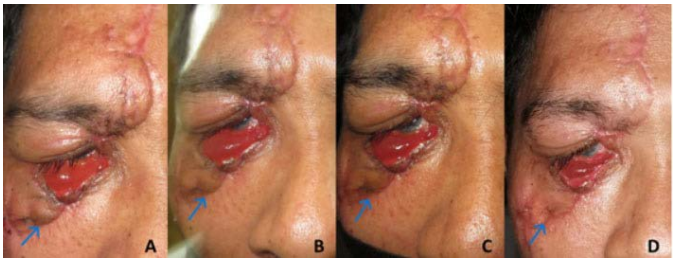

Figure 1: Progressive clinical improvement following intralesional injection of a mixture of 0.3 mL 5-fluorouracil (5-FU, 15 mg) and 0.1 mL triamcinolone acetonide (TA 10%, 1 mg) in a 3:1 ratio, administered to both the superior and inferior eyelids. (A) First injection, (B) Second injection, (C) Third injection, (D) Fourth injection, showing significant reduction in scar height (blue arrow).

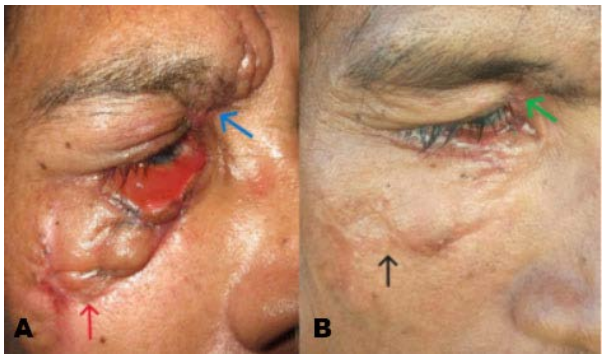

Figure 2: Comparison of clinical appearance before and six months after treatment. (A) Pre-treatment condition showing significant keloid traction of the upper eyelid margin (blue arrow) and an extensive hypertrophic scar on the lower eyelid (red arrow), extending to the cheek area. (B) Six months after completion of intralesional 5-fluorouracil (5-FU) and triamcinolone acetonide (TA) injections, showing marked clinical improvement with resolution of upper eyelid.

DISCUSSION

Ectropion represents a combination of anatomical and functional abnormalities of the eyelid. Cicatricial ectropion, as demonstrated in the present case, may develop secondary to previous trauma and surgical management. The condition can occur in various clinical settings, leading to disabling symptoms and even severe complications such as corneal ulceration, globe perforation, and blindness. Similarly, the present case features severe conjunctival exposure, chemosis, and keratopathy, which cause blindness in the affected eye. Therefore, restoration of eyelid-globe apposition is the main goal of treatment to protect the ocular surface and prevent further complications.

Managing complex periorbital scar contractures requires integrating biological tissue modification with mechanical reconstruction. Hypertrophic scars and keloids are fibroproliferative disorders driven by persistent inflammation, dysregulated extracellular matrix turnover, and overexpressed TGF-β signaling, forcing dermal fibroblasts to synthesize excessive type I and III collagen [6, 7]. Although surgical release with full-thickness skin grafting is commonly used for cicatricial ectropion, surgery in an active fibrotic bed may increase the risk of graft contracture, shrinkage, and recurrence [1]. Preoperative scar modulation may therefore improve tissue pliability and create better conditions for reconstruction.

Several modalities have been described for scar management, including pharmacologic agents, compression therapy, laser treatment, 5-FU, bleomycin, radiotherapy, and intralesional corticosteroid injections. However, optimal outcomes often require the synergistic effect of combined therapies [3]. The use of antineoplastic agents in scar modification is supported by evidence that keloids and hypertrophic scars are associated with hypermetabolic fibroproliferative activity. In vitro and in vivo studies have shown that 5-FU can inhibit collagen synthesis and fibroblast proliferation [5]. As a pyrimidine analog, 5-FU inhibits DNA synthesis by disrupting thymidine production, thereby affecting rapidly proliferating cells such as fibroblasts and facilitating scar remodeling [2]. Furthermore, Wendling et al. reported that 5-FU may selectively block collagen type I fibers, while its antiangiogenic properties may contribute to reduced keloid growth and recurrence when used at non-toxic doses, as described by Ren et al. [4].

The rationale for combining 5-FU with TA is pharmacologically plausible because both agents target complementary components of pathologic scar formation. 5-FU acts primarily as an antifibrotic agent by inhibiting fibroblast proliferation, collagen synthesis, and extracellular matrix production. In contrast, TA suppresses inflammatory scar activity and steroid-responsive fibroproliferative signaling. Despite their different mechanisms, the combination of 5-FU and TA may contribute to cell cycle arrest, downregulation of vascular endothelial growth factor, and inhibition of collagen type I and matrix metalloproteinase-2 synthesis [4]. This complementary mechanism is clinically relevant in periocular scars, where both active inflammation and mechanical contracture contribute to eyelid malposition.

In the present case, the 3:1 mixture of 5-FU and TA was selected as a modified periocular regimen intended to preserve the antifibrotic predominance of 5-FU while limiting absolute corticosteroid exposure. Specifically, the admixture shown in Figure 1 (0.3 mL 5-FU 50 mg/mL plus 0.1 mL TA 10 mg/mL) delivers 15 mg of 5-FU and only 1 mg of TA per aliquot. Thus, although the volume ratio differs from the classic Fitzpatrick protocol, the steroid burden in our case remained low. This consideration is important in eyelid scars because the thin periocular skin is especially susceptible to steroid-related complications such as cutaneous atrophy, telangiectasia, and dyspigmentation. Therefore, our intent was not to use a steroid-dominant regimen, but rather to employ a low-dose adjunctive corticosteroid within a 5-FU-based antifibrotic strategy [4, 5, 8, 9].

Previous studies have investigated the effectiveness of combined 5-FU and TA therapy for keloid and hypertrophic scar management. This interest has largely emerged because conventional intralesional steroid therapy combined with excision has shown variable success rates, ranging from 58% to 93%, with high failure rates and inconsistent therapeutic outcomes in several studies. Steroid-related adverse effects, including telangiectasis, hypopigmentation, and skin atrophy, have also been reported in up to 37% of cases [5]. A meta-analysis by Ren et al. showed that combined TA and 5-FU regimens significantly improved scar recovery compared with TA monotherapy. Similarly, Srivastava et al. reported faster scar flattening and fewer side effects with the combination regimen [4, 8]. These findings support the use of 5-FU/TA as a steroid-sparing approach, especially in anatomically delicate areas such as the eyelids.

Injection protocols vary widely across the literature, including differences in concentration, total number of injections, and treatment intervals. According to the meta-analysis by Ren et al. (2017), several studies used TA 4 mg mixed with 5-FU 45 mg at one-week intervals for a total of eight sessions. Another report used TA 1 mg mixed with 5-FU 45 mg twice weekly for ten sessions. Sensitivity analysis suggested that variations in injection concentration and interval did not significantly affect comparative effectiveness [4]. Occleston et al. also reported broad variation in total injections and intervals, ranging from 1 to 25 injections, with an average of 5–10 sessions and intervals varying from weekly to every three weeks [10]. In the present case, four injection cycles were administered at monthly intervals. This schedule was informed by previous reports showing benefit with repeated 5-FU/triamcinolone injections at approximately four-week intervals and by experimental evidence suggesting sustained antifibrotic effects over several weeks [11]. In addition to this literature-based rationale, treatment continuation was guided by

serial clinical reassessment of the scar before surgery. The endpoint for proceeding to reconstruction was not a fixed numerical threshold, but a clinically meaningful reduction in scar height and induration together with improved pliability of the periocular tissue, indicating a more favorable surgical bed.

The timing of injection was also clinically relevant. Fitzpatrick (1999) reported that symptomatic scars, particularly inflamed, indurated, and erythematous lesions, responded more significantly to injection than inactive scars. In addition, one month was considered the earliest interval after surgery at which postoperative scars may show signs of activity, making it an appropriate time to initiate injection therapy [9]. In this case, injection was initiated one month after the first surgery, when the scar area showed redness and itching, suggesting active scar remodeling. This timing may have allowed pharmacologic intervention during the biologically active phase of scar maturation, before definitive mechanical reconstruction was attempted.

Regarding injection technique, several authors have described pain control methods, including lignocaine as a separate injection or mixed with the treatment solution. Srivastava et al. argued that dilution increases injection volume, which may cause greater tissue stretch and pain, and may theoretically reduce the active drug dose at the target site [8]. Therefore, in the present case, the medications were administered in their original undiluted form without anesthetic agents. Similarly, xylocaine was not added, consistent with previous reports suggesting that pain is primarily caused by the injection procedure itself [9].

After four injection cycles, serial clinical examination and photographic comparison showed a clear reduction in scar prominence, accompanied by subjective softening of the scar and improved mobility of the adjacent periocular tissue. However, these changes were assessed clinically rather than with a validated instrument such as the Vancouver Scar Scale, Patient and Observer Scar Assessment Scale (POSAS), or quantitative lid tension testing. These findings are consistent with the comparative study by Srivastava et al., which reported fewer adverse effects, particularly telangiectasis and atrophy, in the 5-FU + TA group compared with TA monotherapy [8]. In this case, improved tissue pliability appeared to facilitate subsequent surgical release and tissue rearrangement, although a direct causal relationship cannot be established from a single case.

To address the severe cicatricial ectropion, intralesional therapy was followed by surgical reconstruction using multiple Z-plasty. At the time of surgery, the lower eyelid tissues appeared less rigid and more amenable to flap mobilization than at initial presentation, although residual subcutaneous cicatricial tissue still required excision. Because no objective intraoperative tension measurement was performed, this observation should be interpreted as a clinical impression rather than a quantified endpoint. Multiple Z-plasty was selected over skin grafting because the recipient site contained extensive subcutaneous fibrosis, raising concerns regarding vascularity, graft survival, secondary contracture, and postoperative contour mismatch. Z-plasty offered the advantage of redistributing tension vectors, lengthening the contracted scar band, and preserving local vascularized tissue, which are important considerations in periocular reconstruction. This approach is comparable to the report by Deswal et al., in which 4 of 15 patients required surgery to correct cicatricial ectropion after receiving six injections. Among these patients, three underwent full-thickness skin grafting and one underwent lateral tarsal strip surgery. Approximately three additional 5-FU injections were administered at two-week intervals after surgery, resulting in greater graft absorption and reduced scarring. Davidson also reported an average 92% reduction in lesion size among patients treated with combined 5-FU/steroid therapy and excision, while patients treated without excision showed an average 81% reduction [5, 11].

The present case highlights the potential role of staged management in severe cicatricial ectropion associated with active periocular scarring. Rather than proceeding directly to reconstructive surgery in a rigid fibrotic bed, serial 5-FU/TA injections were used to reduce scar activity and improve local tissue characteristics before definitive mechanical correction. This strategy may be particularly useful when full-thickness skin grafting is less desirable because of poor recipient-bed vascularity or extensive subcutaneous fibrosis. However, further studies are needed to determine the optimal concentration, interval, and number of injections for periocular scar modulation.

Several limitations should be acknowledged. First, this report describes a single patient, which limits generalizability. Second, objective scar assessment tools such as the Vancouver Scar Scale or POSAS were not applied, and no standardized photographic grading or quantitative lid tension testing was performed. Therefore, improvement in scar pliability and surgical ease was based on serial clinical observation rather than formal measurement. Third, histopathological evaluation of scar remodeling was unavailable. Finally, the relative contribution of intralesional therapy and surgical reconstruction cannot be separated. In addition, the follow-up period was limited to six months, which may be insufficient to capture late recurrence of cicatricial ectropion or delayed scar contracture during longer-term remodeling. Nevertheless, the marked clinical improvement observed in this case suggests that combined 5-FU/TA scar modulation followed by multiple Z-plasty may represent a useful staged approach for selected patients with severe cicatricial ectropion.

CONCLUSION

In conclusion, the combined use of intralesional 5-FU and TA followed by Z-plasty may represent a promising

staged approach for severe cicatricial ectropion in selected patients. In this case, the treatment was associated with improved scar appearance, better tissue pliability, and favorable functional and aesthetic outcomes during six months of follow-up. However, the findings should be interpreted cautiously given the single-patient design, lack of quantitative scar scoring, and limited follow-up duration, and further studies are required to establish long-term efficacy and recurrence risk.

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Artificial Intelligence (AI) Disclosure

The authors declare that this manuscript was prepared entirely without the use of generative AI.

Author Contributions

Andi Pratiwi – Conception of the work, Acquisition of data, Analysis of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Halimah Pagarra – Design of the work, Acquisition of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Suliati Amir – Acquisition of data, Analysis of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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