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Journal
Dermatology Online Journal, 27(7)

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Publication Date
2021

DOI
10.5070/D327754381

Intralesional 5-fluorouracil utilizing abbreviated tourniquet device in patients with overlying stasis dermatitis or lymphedema

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Keywords: 5-fluorouracil, lymphedema, non-melanoma skin cancer, stasis dermatitis

To the Editor:

Non-melanoma skin cancers (NMSCs) found on the lower extremities present a treatment conundrum for dermatologists that is related to poor healing in this anatomical area [1,2]. The healing process may be further delayed or even complicated if the NMSC exists on a background of stasis dermatitis or lymphedema [1,2]. Stasis dermatitis is a cutaneous manifestation of chronic venous insufficiency (CVI), occurring in 2-6% of the population in the United States [1,3,4]. There are multiple etiologic factors contributing to CVI, including venous hypertension and incompetent venous valves [1,3-5]. Stasis dermatitis is a critical diagnosis to recognize, as patients typically have prolonged wound healing secondary to fibrin cuffing, local edema, and decreased venous return with venous congestion [4,5]. Owing to the high incidence of both stasis dermatitis and NMSC in the United States, it is very common for a patient to have both diagnoses concurrently. Another confounding diagnosis is lymphedema, which is most often acquired from insult to the lymphatic chain and frequently found in conjunction with venous insufficiency [4,5]. The compromise of lymphatic drainage leads to a pathologic accumulation of interstitial fluid, proteins, and inflammatory cells [5]. The chronic microvascular damage that occurs in both stasis dermatitis and lymphedema creates an environment unsuited for surgical excision and the subsequent healing process [5].

Although surgical excision is the first line treatment option for NMSCs, the presence of stasis dermatitis or lymphedema of the lower extremities makes surgical defects particularly difficult to heal. Intralesional 5-fluorouracil (ILFU) and other chemotherapeutic agents, such as methotrexate and bleomycin, have emerged as viable options to treat NMSCs [6-9]. Reasons to support ILFU are clinical efficacy, decreased cost, and patient satisfaction [4,6,9]. Intralesional 5-fluorouracil is an advantageous alternative treatment under certain circumstances, such as for patients who are poor surgical candidates, have multiple NMSCs, exhibit medical comorbidities, or have lower extremity tumors which are associated with impaired healing [7-9]. Intralesional 5-fluorouracil has been reported to be more effective when compared to other chemotherapeutic entities [8,9]. Maghfour et al. found that ILFU used at concentrations ranging from 30-50mg/ml demonstrates clearance rates of 91% for basal cell carcinoma (BCC), 87% for squamous cell carcinoma (SCC), and 74.5% for keratoacanthoma (KA). The majority of groups discussed by Maghfour et al. used the standard 50mg/ml concentration of 5-FU without dilution; however, one single study utilized a gel formulation of 5-FU at a concentration of 30mg/ml [8]. Additionally, recurrence rates were reliably low for all three varieties of NMSC: 0% for BCC, 0.5% for SCC, and 1.15% for KA [8].

Adverse effects of ILFU include pain, stinging, or burning during injection, erythema, dyspigmentation, swelling, ulceration, or necrotic involution of the tumor [6,8]. Notably, large review studies have not encountered systemic adverse effects with ILFU [8]. In patients with stasis dermatitis or lymphedema, there is a concern for extravasation of the chemotherapeutic agent outside of the target area, which may result in tissue necrosis. This risk of extravasation relates to the increased hydrostatic pressure associated with venous insufficiency causing capillary damage and local edema.

Although ILFU has emerged as a durable alternative treatment for NMSC on the lower extremities, we have observed severe skin necrosis associated with extravasation of ILFU in patients with stasis dermatitis or lymphedema (**Figure 1**). This report demonstrates that in patients with significant local edema, the novel use of an abbreviated tourniquet device during injection of ILFU may prevent extravasation of the chemotherapeutic agent and decrease the risk of local necrosis. Ultimately, this will help prevent complications of ILFU and assist in treatment and healing of NMSC following injection of the chemotherapeutic agent.

Prior to treatment, the NMSC is identified on the lower extremity of a patient with stasis dermatitis or lymphedema. We typically guide injection volume of ILFU by the diameter of the clinical lesion: 0.2ml (final concentration 25mg/ml) for ≤0.5 cm, 0.3ml (final concentration 30mg/ml) for 0.6 cm-0.9cm, and 0.4ml (final concentration 33.3) for ≥1.0cm diameter. We elected to use the finger loop of a needle driver for the abbreviated tourniquet device based on size and shape. The device is placed over the lesion on the lower extremity and held in place for thirty seconds prior to injection, providing circumferential compression. A 30-gauge needle is used to inject a volume of 0.4ml of 5-FU 50mg/ml mixed with 0.2ml of lidocaine without epinephrine intralesionally, for a final concentration of 33.3mg/ml (**Figure 2**). The device is then removed thirty seconds after injection is completed. Patients return for follow-up two weeks post-procedure to measure clinical improvement and assess if a subsequent treatment is required. Patients are educated on wound care and signs of necrosis and are given written care instructions to take home. Patients are advised to self-administer acetaminophen or ibuprofen in four-hour intervals for pain management as needed. It is recommended to avoid ice or cold compresses as

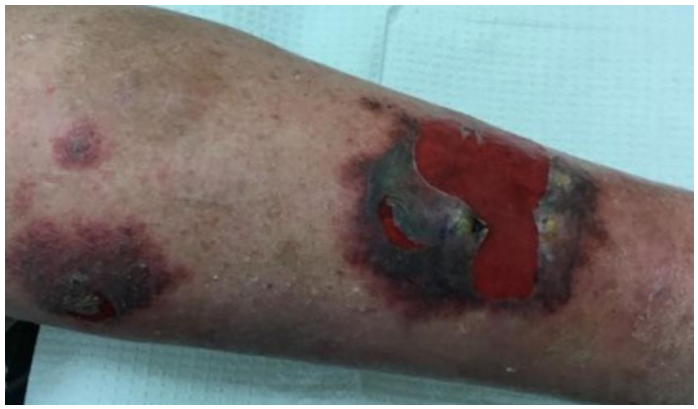

Figure 1. *Patient was treated with a standard dose of 0.4ml of 5-fluorouracil 50mg/ml mixed with 0.2ml of lidocaine without epinephrine (for a final concentration of 33.3mg/ml) to treat a squamous cell carcinoma on the right lower extremity. Patient presented one week status post intralesional 5-fluorouracil injection with local skin necrosis secondary to underlying stasis dermatitis causing extravasation of chemotherapeutic agent.*

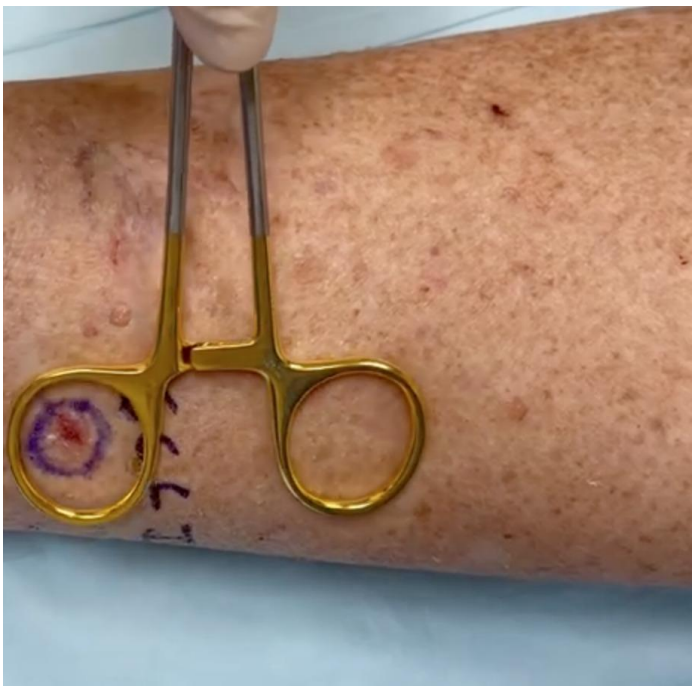

Figure 2. *The finger loop of a needle driver measuring 2.5×3.0 cm is placed directly over a biopsy-proven non-melanoma skin cancer and held in place for thirty seconds prior to injection. A 30-gauge needle is used to intralesionally inject a volume of 0.4ml of 5-fluorouracil 50mg/ml mixed with 0.2ml of lidocaine without epinephrine (for a final concentration of 33.3mg/ml). The finger loop is removed thirty seconds after the completion of injection.*

this may cause decreased blood flow to the injection site. Finally, patients are instructed to call the office for uncontrolled bleeding, pain unresponsive to analgesia, erythema, or necrosis. It is critical that patients are educated about warning signs to reduce the risk of necrosis or secondary infection.

We have performed this technique successfully with empirical evidence that the abbreviated tourniquet device may reduce the risk of medication diffusion into surrounding tissue and subsequent local necrosis in patients with stasis dermatitis or lymphedema. However, controlled studies are required to demonstrate true efficacy and compare with other methodology.

Over the past decade, ILFU has emerged as an efficacious and cost-effective alternative therapy to treat NMSC on the lower extremities [6,7,9]. Owing to local edema and poor venous return, patients with stasis dermatitis or lymphedema are at risk of necrosis secondary to local extravasation if treated with ILFU [8]. The use of an abbreviated tourniquet device during ILFU injection for NMSC on the lower extremities may decrease this risk and offer improved outcomes in these patients.

Potential conflicts of interest

The authors declare no conflicts of interest.

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