To order reprints or e-prints of JDD articles please contact sales@jddonline.com

Copyright © 2018 BRIEF COMMUNICATION Journal of Drugs in Dermatology

Intralesional 5-Fluorouracil in the Treatment of Lower Leg Squamous Cell Carcinoma

Morgan Mackey DO,[a] Adam Shahsavari DO,[b] V. Thomas Mackey DO[a]
[a]Advanced Desert Dermatology, Peoria, AZ and the Osteopathic Postdoctoral Training Institution (OPTI) at Midwestern University, Glendale, AZ
[b]Larkin Palm Springs Community Hospital, Hialeah, FL

ABSTRACT

Non-melanoma skin cancer (NMSC) is the most commonly diagnosed cancer in the United States.[1,2] There are different treatment modalities for non-melanoma skin cancer, that include surgical excision, radiation therapy, cryotherapy, electrodessication and curettage, photodynamic therapy, and topical chemotherapy. Intralesional injection with 5-fluorouracil is a treatment modality that is not used often, perhaps due to not much research available to its effectiveness or established treatment recommendations. We report a case of a patient with multiple lesions of cutaneous squamous cell carcinoma on the lower extremities treated successfully with intralesional 5- fluorouracil.

J Drugs Dermatol. 2018;17(11):1241-1243.

INTRODUCTION

Non-melanoma skin cancer (NMSC) is the most commonly diagnosed cancer in the United States.[1,2] While the prevalence of NMSC is continually elevating the overall treatment of choice remains to be surgical intervention. Surgical operations comprised over 95% of all basal cell carcinoma treatments within the United States.[3] While this treatment style remains a staple to NMSC treatment it is not feasible in all situations due to wound closure issues, graft rejection, increased lesion size, or poor perfusion at the treatment site.[4]

In a patient whose clinical picture contains multiple aforementioned criteria, a less invasive treatment method is more likely to lead toward a favorable outcome. Non-surgical options include photodynamic therapy, immunotherapy, topical chemotherapy, radiation therapy, and intralesional therapies. Intralesional therapies have been explored, which primarily include interferon, bleomycin, 5-fluorouracil, and methotrexate.[5] We report a case of the use of intralesional 5-fluorouracil for treatment of squamous cell carcinoma of the lower extremities.

Case Report

An 86-year-old female presented with a past medical history significant for hyperlipidemia, hypertension, atrial fibrillation, transient ischemic attack, breast cancer, lung cancer, osteoporosis, joint replacement of the left hip, double mastectomy, previous ankle surgery requiring placement of metal plate, poor circulation of her lower extremities, previous cutaneous squamous cell carcinoma of the left lower leg, previous smoker, and multiple erythematous tender papules with hyperkeratotic scale distributed throughout her lower legs. Sites of these lesions include the right proximal lateral pretibial skin, right proximal pretibial skin, left lateral ankle, and right distal lateral pretibial skin (Figures 1 and 2). Patient had a total of six lesions biopsied, with five of these lesions diagnosed histologically as well-differentiated squamous cell carcinoma and the left lateral ankle lesion diagnosed histologically as atypical cystic squamous proliferation.

The patient's history is significant for a squamous cell carcinoma of the lower extremity in the past that was excised, and afterwards required multiple wound clinic treatments and took almost one year to heal. With six new SCC lesions of the lower extremities found, there was concern about the healing of each of these spots if they were to be treated with excision. Thus, treatment with intralesional 5-fluorouacil was chosen as biopsy would be done post treatment to show results of this treatment.

Treatment was initiated with intralesional injections of 5-fluorouracil. 5-Fluorouracil was administered via a 50mg/mL solution for a total of 0.6 milliliters at each lesion. All six lesions received 30mg of fluorouracil per treatment for a total course of six treatments on a weekly basis. Post-treatment biopsies were taken from the lesions and revealed complete resolution of squamous cell carcinoma at all treatment sites (Figure 3). Patient has been followed for 3 months after finishing treatment and has had no recurrence seen on exam. Patient reported no fatigue, diarrhea, mouth sores, eye irritation, headache, poor appetite, or other systemic side effects associated with the treatment of 5-fluorouracil.

JOURNAL OF DRUGS IN DERMATOLOGY JDD
Do Not Copy Penalties Apply
This document contains proprietary information, images and marks of Journal of Drugs in Dermatology (JDD).
No reproduction or use of any portion of the contents of these materials may be made without the express written consent of JDD.
If you feel you have obtained this copy illegally, please contact JDD immediately at support@jddonline.com
JO01118

To order reprints or e-prints of JDD articles please contact sales@jddonline.com

FIGURE 1. Two squamous cell carcinoma (SCC) lesions on the left lower extremity prior to treatment.

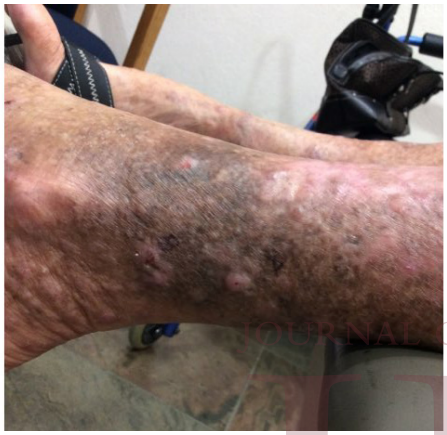

FIGURE 2. Two SCC lesions on the right lower extremity prior to treatment.

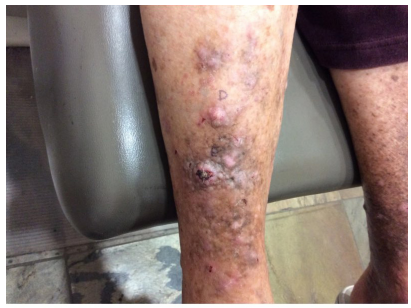

FIGURE 3. Post-treatment of lesions from Figure 2.

DISCUSSION

First-line treatment for NMSC remains surgical intervention, however in situations in which patients are poor surgical candidates, other modalities must be employed. Factors implicated in unfavorable surgical outcomes which lead to prolonged wound healing include a history of hip or knee replacement surgery, an ankle brachial index of less than 0.80, female gender, elderly age, and increased initial lesion size.[4] Further exploration of non-invasive treatment modalities must be explored for this patient population as to not lead to chronic ulcerations. Intralesional therapy with 5-Fluorouracil is an inexpensive, efficacious, and non-invasive method with which to approach these lesions.[3] The cost of a 50-mL vial of 5-Fluorouracil is cited between $19.50-$26.00, with the treatment regimen employed in this case report, up to thirteen lesions could be treated per vial.

5-Fluorouracil's inhibition of thymidylate synthetase and subsequent inhibition of DNA synthesis has led it to become widely utilized in treatment of various malignancies. However, intralesional 5-fluorouracil for NMSC remains a relatively uninvestigated area of non-invasive treatment. This has led to a reduced usage of intralesional therapy, potentially due to the absence of therapeutic guidelines and the existence of few well-designed clinical trials.[5] While the few clinical trials performed have revealed promising results, more investigation is warranted.

A clinical trial performed in 1997 by Miller et al[6] revealed a 91% biopsy-proven cure rate of basal cell carcinoma in patients treated with 0.5 mL of a gel consisting of 5-fluorouracil (30 mg/mL), epinephrine (0.1 mg/mL), and bovine collagen. Treatments regimen consisted of injections of the gel for three times a week for two successive weeks. 5-Fluorouracil has also been implicated in the treatment of squamous cell carcinoma with initial reports of this treatment modality in 1962.[7] A clinical trial consisting of 25 patients reported a 96% cure rate of well-differentiated squamous cell carcinomas. The treatment regimen in this study consisted of 4-6 injections of 1 mL of 5-fluorouracil (30mg/mL). Patients in this study reported good overall cosmesis and no significant side effects.[6]

While most data sets reporting on 5-fluorouracil's intralesional efficacy in NMSC are relatively small they generally show superiority in comparison to the other intralesional agents.[7] While not directly studied head to head, multiple studies have reported superior outcomes of 5-fluorouracil in comparison to methotrexate in the treatment of keratoacanthomas.[3,8] Meta-analysis of other intralesional therapies has shown 5-fluorouracil to have superior cure rates for NMSC in comparison to interferon and interleukin-2.[7]

In conclusion, intralesional use of 5-fluorouracil in NMSC is an inexpensive, efficacious, and non-invasive method of treatment for non-surgical candidates. With the advent of further additional clinical trials and large-scale studies a more pin-point set of clinical guidelines may be created. With greater data sets the ability to determine the optimal dosage and interval of treatment will be elucidated and allow for better future treatment with this modality.

DISCLOSURE

The authors have no conflicts.

This document contains proprietary information, images and marks of Journal of Drugs in Dermatology (JDD).
No reproduction or use of any portion of the contents of these materials may be made without the express written consent of JDD.
If you feel you have obtained this copy illegally, please contact JDD immediately at support@jddonline.com

JO01118

To order reprints or e-prints of JDD articles please contact sales@jddonline.com

REFERENCES

1. Lomas A, Leonardi-Bee J, Bath-Hextall F. A systematic review of worldwide incidence of nonmelanoma skin cancer. *Br J Dermatol.* 2012;166:1069-1080.
2. Rogers HW, Weinstock MA, Harris AR, et al. Incidence estimate of nonmelanoma skin cancer in the United States, 2006. *Arch Dermatol.* 2010;146:283-287.
3. Lauren Metterle, Christopher Nelson, Nishit Patel. Intralesional 5-fluorouracil (FU) as a treatment for nonmelanoma skin cancer (NMSC): A review. *J Am Acad Dermatol.* 2016:74:552-557.
4. Margolis DJ, Berlin JA, Strom BL. Risk Factors Associated with the Failure of a Venous Leg Ulcer to Heal. *Arch Dermatol.* 1999;135:920–926.
5. Joslyn S. Kirby, Christopher J. Miller. Intralesional chemotherapy for nonmelanoma skin cancer: A practical review. *J Am Acad Dermatol.* 2010;63:689-702.
6. B.H. Miller, J.S. Shavin, A. Cognetta, et al. Nonsurgical treatment of basal cell carcinomas with intralesional fluorouracil/epinephrine injectable gel. *J Am Acad Dermatol.*1997;36:72-77.
7. Laurie M. Good, Misha D. Miller, Whitney A. High. Intralesional agents in the management of cutaneous malignancy: A review. *J Am Acad Dermatol.* 2010;64:413-422.
8. Nicole M. Annest, Marta J. VanBeek, Christopher J. Arpey, et al. Intralesional Methotrexate treatment for keratoacanthoma tumors: A retrospective study and review of the literature. *J Am Acad Dermatol.* 2007;56:989-993.
9. Vishwas Parekh, John T. Seykora. Cutaneous Squamous Cell Carcinoma. *Clin Lab Med.* 2017;37:503-525.

AUTHOR CORRESPONDENCE

Morgan Mackey D.O.
E-mail:.....mmackeydo@gmail.com

JOURNAL OF DRUGS IN DERMATOLOGY
JDD
DRUGS • DEVICES • METHODS

Do Not Copy
Penalties Apply

This document contains proprietary information, images and marks of Journal of Drugs in Dermatology (JDD).
No reproduction or use of any portion of the contents of these materials may be made without the express written consent of JDD.
If you feel you have obtained this copy illegally, please contact JDD immediately at support@jddonline.com

JO01118