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Case Report

Neoadjuvant Intralesional Treatment of SCC with 5-FU: A Case Report

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Abstract

5-Fluorouracil (5-FU) has been used topically and intralesional to treat lesions related to squamous cell carcinoma (SCC) such as actinic keratosis, Bowen's disease, and keratoacanthoma.

This case of squamous cell carcinoma (SCC) that was successfully treated with intralesional 5-FU, provides a possible therapeutic option for patients who are not good surgical.

Keywords: 5-Fluorouracil (5-FU); Squamous Cell Carcinoma; Keratoacanthoma

Introduction

5-Fluorouracil (5-FU) has been used topically and intralesional to treat lesions related to squamous cell carcinoma (SCC) such as actinic keratosis, Bowen's disease, and keratoacanthoma.

Case Report

A female patient, 84 years old, with no history of any important antecedents or comorbidities. Was studied six months ago, she was presented to our clinic in the department of Dermatology, with two tumoral lesions on her face. They had an aspect of infiltrated plaques, that have experienced painless and gradual growth in size over the past two years, and have started to spread locally.

On physical examination, an infiltrated plaque with irregular borders, measuring 3.5 cm x 1.5 cm was located on the upper lip. Another lesion was on the left cheek (Figure 1).

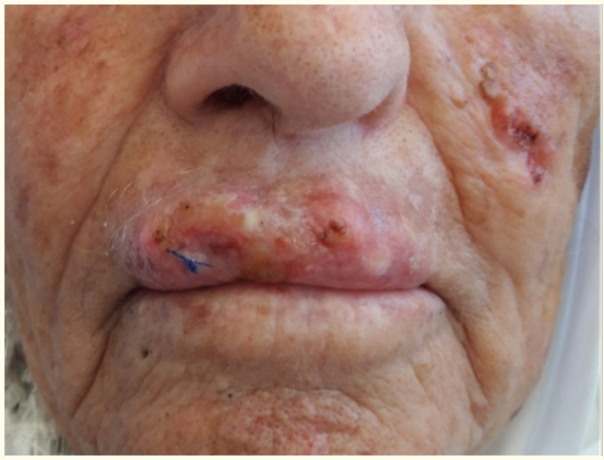

Figure 1

Also, two palpable lymph nodes were noticed on both sides of the neck. The rest of the examination was normal. The initial clinical diagnosis was cutaneous SCC. Then, an incisional biopsy was taken and confirmed the diagnosis of SCC, grade II (Figure 2).

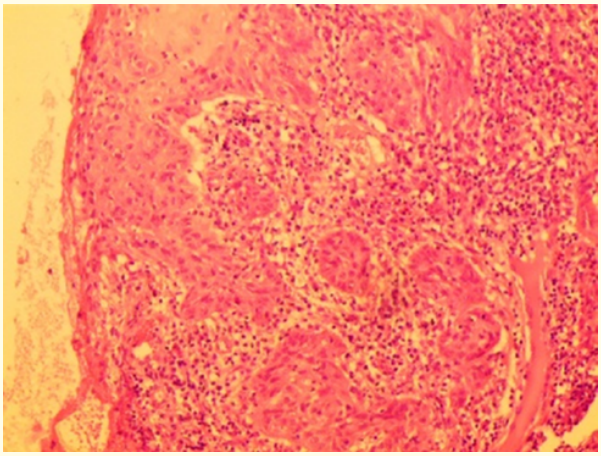

Figure 2: Microscopic images of the lesions show nests of atypical epidermal cell proliferation with anaplasia, and central keratinization.

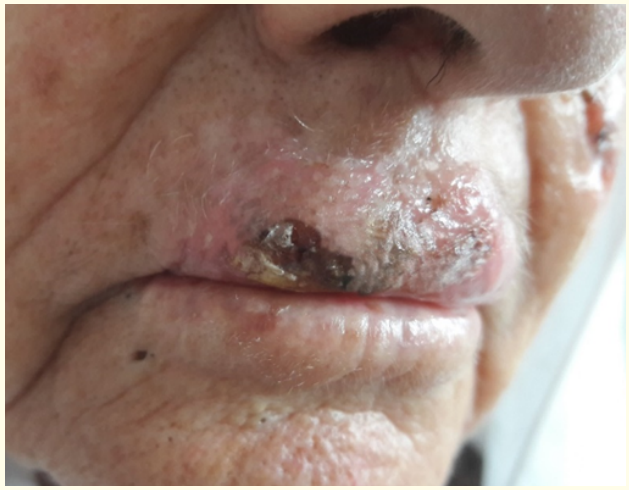

Figure 3: After final session of 5-FU injection.

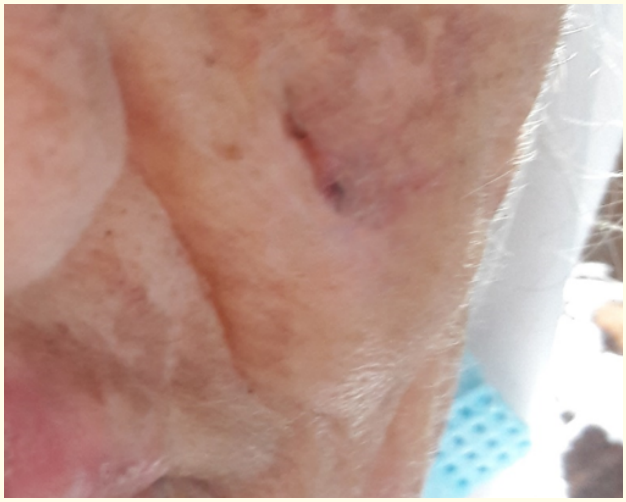

Figure 4: After final session of 5-FU injection.

CT (Computed Tomography) of the neck showed lymphadenopathy in two nodes measuring 1 cm and 7 mm. CT scan of the chest showed calcifications in the upper and middle lobes of the left lung. CT of the abdomen, and pelvis, full blood count, and liver and renal functions were normal.

After consulting with the surgeon, it was decided to begin with neoadjuvant chemotherapy in order to reduce the mass to facilitate the excision. The patient underwent five sessions of intralesional 5-FU 50 mg. Each session consisted of injecting the lesion with equal amounts of 5-FU in 4-5 separate sites. The sessions were done every week. After each session, a reduction in the size of the tumor was noted. (Figure 3 and 4) during the chemotherapy cycles, all hematological parameters were stable, and no serious side effects were observed. After finishing the chemotherapy, the tumor diminished tremendously, and the patient was sent for surgery.

Results and Discussion

Non-melanoma skin cancer is the most common malignant neoplasm diagnosed in white individuals in the United States. The American Cancer Society estimates that over 1 million new cases occur annually. Most patients receive successful local therapy. Death from the disease is very rare, with a case-fatality rate of 0.25% (approximately 2000 cases per year) [1].

Cutaneous Squamous Cell Carcinoma (cSCC) represents approximately (15%) of all non-melanoma skin cancers. cSCC has a poor prognosis, especially if it invades the lymph nodes and adjacent vital structures. Actinic keratosis is the premalignant precursor for cSCC, and early treatment will save the patient's morbidity. Other risk factors, such as ultraviolet light from sun exposure, are linked to cSCC, while intrinsic factors, such as the use of antioxidants, as-

pirin, and nonsteroidal anti-inflammatory drugs (NSAIDs), are reported to reduce the risk of developing the disease [2].

Clinically, cSCC presents as an ulcerated plaque with elevated margins, and usually located in a sun-exposed area. Typical surface changes may include scaling, deep bleeding ulceration, crusting, and cutaneous horn [2].

Diagnostic workup of suspected cSCC will include computed tomography (CT) scanning to evaluate the degree of the invasion to the deep tissues and lymph node metastasis. Magnetic resonance imaging (MRI) may be used to rule out invasion of neural structures. Incisional or excisional biopsy are essential for definitive diagnosis. The choice of biopsy will depend on the size and location of the lesion [2].

The most common treatment of this malignancy is surgery. However, because SCC often occurs on areas of the face, ears, neck, and dorsal surfaces of the hands and arms, patients are frequently concerned about scarring. Thus, an alternative treatment is desirable for patients who prefer nonsurgical treatment or who are not good surgical candidates. Other treatment options include the following: Mohs micrographic surgery for invasive type of cSCC in the facial region, treatment with radiotherapy as an adjuvant to surgery, to provide improved locoregional control, or as primary therapy in patients who are unable to undergo surgical excision; systemic chemotherapy for metastatic cSCC; local chemotherapy with intratumoral fluorouracil (5-FU) injectable gel was evaluated as a nonsurgical approach for treating primary squamous cell carcinoma (SCC) of the skin [3].

5-FU is a structural analogue of thymine that interferes with DNA synthesis and results in death of rapidly proliferating malignant cells. It has been used topically to treat some skin lesions such as actinic keratosis, Bowen's disease, and superficial basal cell carcinoma [4]. 5-FU has also been used intralesionally in the treatment of keratoacanthomas (KAs) [5-8] and nodular basal cell carcinomas [9]. In 1962, Klein., *et al*. were the first to demonstrate successful treatment of KAs with intralesional 5-FU. Since then, there have been numerous reports of KAs safely and effectively treated with intralesional 5-FU [5-8].

In two separate studies, a total of 55 lesions located on sun-exposed areas of the face, head, and extremities were studied. Fifty-three of the 55 lesions (96%) showed histologic clearing after an average of three weekly injections of 0.2 to 0.6mL of an aqueous solution of 50 mg/cm^3 5-FU [5,6]. In another case report, a patient with 14 KAs experienced total clearing of his lesions with slightly smaller doses (0.1 to 0.2 mL) over a longer period of time (five to nine weekly injections) [5].

Other published articles studied the effect of 5-FU on BCC. A systematic review found that fluorouracil produced clearance rates of 90% for superficial BCC, but 97% of patients experienced adverse effects such as erythema, pruritus and pain [10]. In a trial that compared the effectiveness of topical PDT with imiquimod or fluorouracil in patients with superficial BCC, the cure rate for MAL-PDT was 72.8%, for imiquimod 83.4% and for fluorouracil 80.1% [11].

In a 1997 open-label randomized study of 116 subjects with nodular or sBCC, Miller., *et al*. compared six regimens of intralesional 5-FU with epinephrine gel. Meaningful histologic clearance resulted 3 months posttreatment across all study arms (overall histologic clearance rate 91%, 95% CI 84 - 96). There were no statistically significant differences between regimens, but all participants receiving 0.5 ml 5-FU/epinephrine gel 39/week for 2 weeks had histologic cure, leading the authors to conclude that this was the optimal regimen.

In 1997, a study compared two doses and four treatment schedules of 5-FU/epi gel in an open-label, randomized study of 122 patients with biopsy-proven BCCs. One BCC per patient was treated for up to 4 to 6 weeks, then observed for 3 months at which time the tumor site was completely excised for histologic examination. Overall, 91% of evaluable treated minors (106 of 116) in all regimens had histologically confirmed complete tumor resolution. No clinically significant treatment-related systemic adverse events occurred. The best response rate, tolerance, and patient compliance with assigned dose were in patients receiving 0.5 ml of 5-FU/epi gel three times a week for 2 weeks. The complete response rate based on histologic assessment in this group was 100% [9].

Given the histologic similarities between KAs, BCCs, and well-differentiated SCC, it would follow that 5-FU might be effective in the treatment of SCC and its related precursors.

A review of the literature indicates that only a few reports of the use of intralesional 5-FU in the treatment of SCC has been published. In one study [3], 23 patients with biopsy-proven SCC were treated with intratumoral 5-FU/epinephrine gel, with 96% having histologically confirmed complete tumor clearing. These tumors of less than 6 months' duration were located on the face, head, neck, trunk, arms, or hands and ranged in size from 0.24 to 7.50 cm. The

patients received four to six weekly intralesional injections of 1.0 mL or less of a combination of 30 mg/mL of 5-FU and 0.1 mg/mL of epinephrine gel. Only 1 of 23 failed treatment with residual focal Bowen's disease. All patients received a good to excellent cosmetic result.

In another study, a patient with SCC at the junction of the right alar crease and right nasolabial fold was treated with eight weekly injections of 5-FU, with doses ranging from 0.8 to 2.4 mL. A repeat biopsy after the eighth treatment showed total clearance of the cancer, and the patient has remained free of recurrence during a 5-month follow-up period [12].

In a study published in 2000, eight patients affected by conjunctival squamous cell carcinoma (three recurrent cases, three incompletely excised, and two untreated cases) were treated with 1% 5-FU eye drops. Topical 1% 5-FU was administered four times daily for 4 weeks (one course). All patients showed clinical regression of conjunctival carcinoma after topical 1% 5-FU treatment [13].

Notable advantages of intratumoral 5-FU/epi gel are that it is a nonsurgical, tissue-sparing modality with good to excellent cosmetic results that precisely targets the site with high concentrations of the chemotherapeutic agent without systemic toxicity [3].

Conclusion

In this case report, our patient received five weekly injections of 5-FU. The total amount of drug received over the 5 weeks was 250 mg, resulting in a considerable reduction of the cancer, thus becoming a better candidate for skin-sparing surgery. These results along with the proven use of 5-FU in treating lesions related to SCC, demand that further studies should be done on the effectiveness and dosing of intralesional 5-FU in treating SCC. This modality may eventually provide patients with SCC in cosmetically important locations or in areas that require complex surgery the advantage of a nonsurgical cure or a minimally invasive surgery.

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