Successful treatment of squamous cell carcinoma with intralesional methotrexate

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INTRODUCTION

Cutaneous squamous cell carcinoma (cSCC) is associated with several risk factors, including sun exposure, advanced age, fair skin, and immunosuppression.[1] It is the second-most common skin cancer in the United States,[2] with an estimated annual incidence of 700,000 cases,[3] and represents 20% to 50% of skin cancers.[4] While cSCC has a metastatic rate of 2% to 5%,[5] the rate tends to be higher (7.5%) on the lip vermilion.[6]

The treatment of choice for cSCC is surgery; however, nonsurgical options are generally reserved for patients who refuse surgery or cannot tolerate a surgical procedure.[7] The treatments combining surgery with radiotherapy or chemotherapy showed efficiency only in early-stage and well-defined cSCC.[8]

Intralesional 5-fluorouracil, interferon α, and methotrexate have been used sporadically for the treatment of squamous cell carcinoma.[9]

CASE REPORT

A 90-year-old man from Morelia, México, with no significant medical history presented in June 2017 with a 2-cm tumor on the right side of the lower vermilion, extending about 5 mm inside of the oral mucosa. It was indurated and covered by a yellowish crust. The lesion was indolent and had been growing for 18 months. No regional lymphadenopathy was detected on examination (Fig 1).

A punch biopsy showed squamous cell carcinoma with moderate pleomorphism and dyskeratosis with oval and polygonal nuclei with an irregular shape. The tumor infiltrated the entire thickness of the dermis, without vascular permeation and without perineural invasion (Fig 2).

Abbreviation used:

cSCC: cutaneous squamous cell carcinoma

Surgical treatment was declined because of the patient's fear of the cosmetic outcome, so it was decided to treat him with intralesional methotrexate. Methotrexate 25 mg was injected in 1 ml (25 mg) with an insulin needle gauge 30, monthly at 3 separated intervals. The patient had an excellent clinical response with complete resolution (Fig 3). No recurrence was observed at 1 year of follow-up.

Two months after completed treatment, a second biopsy was taken, which revealed mild acanthosis and mild reactive hyperkeratosis in the dermis. An inflammatory process was observed with mature lymphocytes and few plasma cells and hyalinized fibrosis. No residual tumor was observed (Fig 4).

DISCUSSION

Methotrexate is a folic-acid analog that irreversibly inhibits the enzyme dihydrofolate reductase, blocking the synthesis of tetrahydrofolate and, ultimately, preventing the formation of thymidine[9]; likewise, it increases WWOX gene expression, which promotes caspase activation and apoptosis of cSCC cells.[7]

Many cases and series have reported on its effectiveness in treating keratoacanthoma[10]; however, data on intralesional methotrexate in patients with cSCC are scarce.[7,11] Recently, a small observational retrospective trial comparing intralesional

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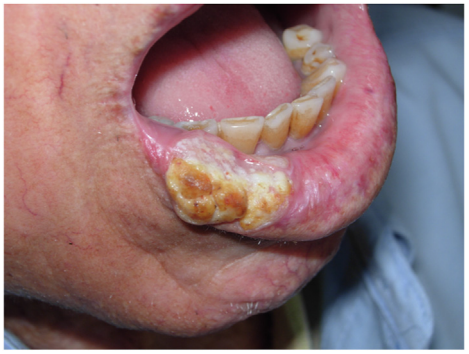

Fig 1. A white-yellowish nodule on the right border of the inferior lip was present on consultation. The tumor extended into the inner border of the lip.

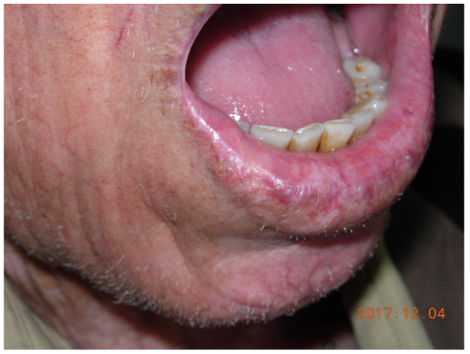

Fig 3. Six months after the first visit, a complete clinical response was observed. No crusty yellowish tumor was observed at the inner border of the lip. *Colorized.

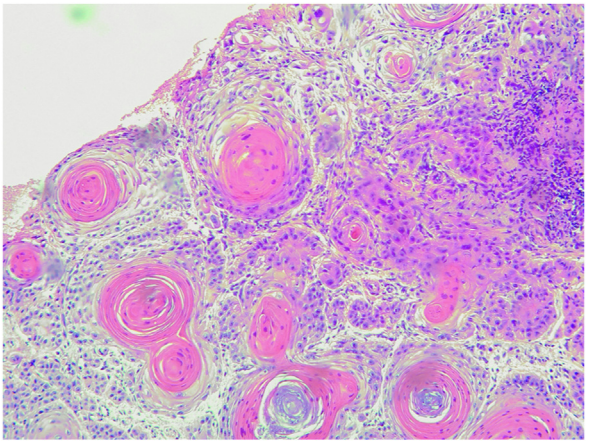

Fig 2. Cutaneous squamous cell carcinoma with dyskeratosis. Well-formed keratinizing structures known as "keratin pearls" were observed on histopathologic examination, as moderate cellular pleomorphism.

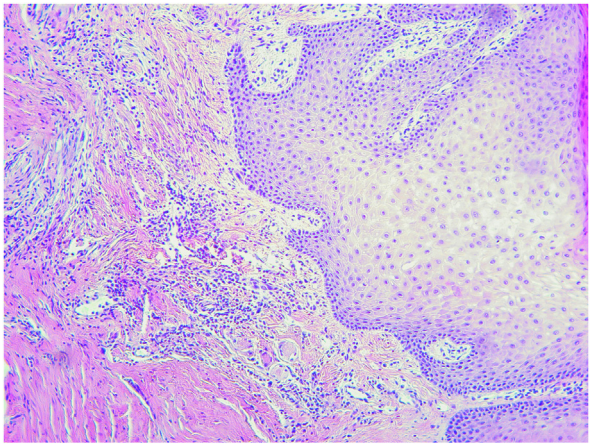

Fig 4. On follow- up biopsy, no tumor was observed; only hyalinized fibrosis, hyperkeratosis, and inflammatory changes were reported on histopathological examination. *Colorized.

methotrexate plus surgery versus surgery alone demonstrated a reduction in tumor size that subsequently could facilitate surgery.[7]

In this patient, methotrexate was well tolerated, had a quick response, and was easily administrated at a low cost. At this time, surgical treatment remains the treatment of choice. Since the patient refused surgery, an alternative was required. Methotrexate therapy was chosen, which showed very good effectiveness. However, data with a greater number of clinical cases and long-term follow-up examinations are necessary before this therapeutic intervention could be recommended as an optional approach.

Conflicts of interest

None disclosed.

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