Medical therapy for keratoacanthomas

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Small keratoacanthomas (KAs) on the trunk and extremities are well suited to surgical excision, and Mohs surgery can produce excellent results for lesions in problematic sites. The authors of the counterpoint article[1] in this issue of *Journal of the American Academy of Dermatology* have done an excellent job of discussing the role of 5-fluorouracil (5FU) injections in the primary treatment of selected patients and prevention of recurrence, but they maintain that surgery remains the criterion standard. I thank them for their willingness to argue one side of the issue to inform our readers, knowing full well that the answer is unique to each patient. My commentary will focus on instances in which medical rather than surgical therapy represents the criterion standard of treatment. Examples include KAs infiltrating into vital structures and widespread eruptive KAs.

KAs can grow quickly and impinge on vital structures including the eyelids, nose, lips, and digits. Perineural invasion occurs with a wide variation in reported incidence but does not appear to affect outcome in most cases.[2,3] Fig 1 shows a patient who presented to Drs. Walter and Dorinda Shelley with a giant KA infiltrating both the upper and lower lips and the nasal philtrum. The patient was treated with oral methotrexate (MTX) in doses similar to those give for psoriasis, with complete resolution of the lesion (Fig 2). Although the cosmetic outcome is not perfect, most of the resulting scar relates to the incisional biopsy, it is amenable to scar revision, and it would be difficult to argue that complete excision of the lesion followed by flap repair could achieve results as good as those achieved with medical therapy. In short, there are instances where surgery is associated with greater morbidity than medical therapy and is the medical option that represents the criterion standard.

Abbreviations used:

5FU: 5-fluorouracil
KA: keratoacanthoma
MTX: methotrexate

Intralesional injection of MTX has been used as an alternative to 5FU injections[4] and is associated with less burning. I typically prescribe 2 mg of folic acid daily for 1 week to reduce the risk of associated nausea when using MTX as an alternative to 5FU. Supplemental Figs 1 and 2 (available via Mendeley at http://doi.org/10.17632/6wpwmkmdt3.2) show a patient with a large KA involving the digit. Such lesions commonly show perineural involvement, and this patient had been scheduled for amputation. Before amputation, an enlightened hand surgeon consulted a dermatologist. The lesion regressed entirely after intralesional MTX injection with sparing of the digit. I believe this patient would argue that medical therapy was the criterion standard and was superior to the surgical option of amputation.

Eruptive KAs (Fig 3) may be associated with an inherited genodermatosis or BRAF inhibition, or they may occur sporadically on the extremities of older individuals. The old quip is that when 1 is excised, "5 come to the funeral," and clinicians and patients alike are often frustrated by the occurrence of multiple eruptive lesions on the extremities after surgical excision. I have seen patients who were referred to an oncologist and scheduled for systemic chemotherapy for "metastatic squamous cell carcinoma" in this setting. It is far better to treat such patients with intralesional 5FU or MTX injection, topical 5FU cream under Unna boot occlusion,[5] systemic acitretin,[6] or a combination.[7] I typically saucerize the largest lesions, infiltrate the base with a

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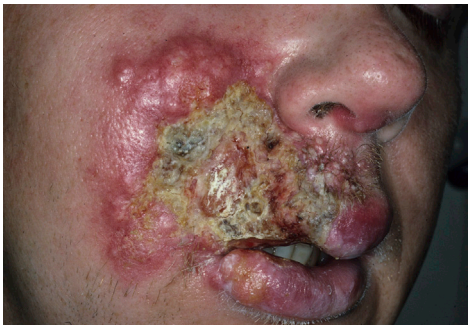

Fig 1. Giant KA involving the upper and lower lips and nasal philtrum. (Image courtesy of Dorinda Shelley. Reprinted with permission from *Cutis*.)

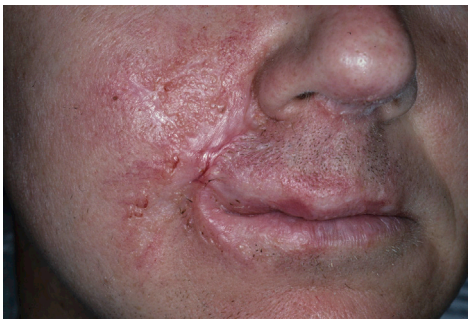

Fig 2. Resolution of giant KA after oral low-dose methotrexate. (Image courtesy of Dorinda Shelley. Reprinted with permission from *Cutis*.)

small amount of 5FU or MTX, and apply a thick coat of 5FU cream and an Unna boot. The "chemoboot" is replaced weekly until all lesions are resolved. Typically, only 1 or 2 applications are necessary.

Again, I would like to thank Drs. Hoegler and Schleichert for their excellent discussion and willingness to argue the other side of this issue. We hope readers will enjoy the point/counterpoint articles in the "Controversies" series and that they will spark healthy debate and further research.

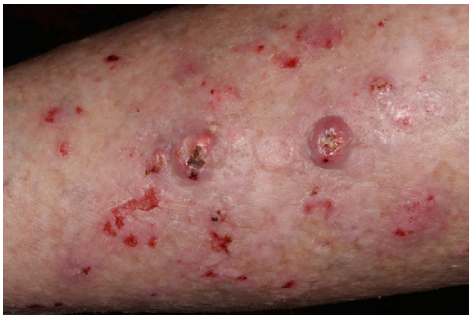

Fig 3. Euptive keratoacanthomas on the leg. The lesions resolved completely with 5-fluorouracil under Unna boot occlusion.

REFERENCES

1. Hoegler KM, Schleicert RA. Is the first-line treatment of keratoacanthomas surgical excision or injection of intralesional chemotherapy? *J Am Acad Dermatol*. 2020;83:1542-1543.
2. Lapins NA, Helwig EB. Perineural invasion by keratoacanthoma. *Arch Dermatol*. 1980;116(7):791-793.
3. Godbolt AM, Sullivan JJ, Weedon D. Keratoacanthoma with perineural invasion: a report of 40 cases. *Australas J Dermatol*. 2001;42(3):168-171.
4. Smith C, Srivastava D, Nijhawan RI. Intralesional methotrexate for keratoacanthomas: a retrospective cohort study. *J Am Acad Dermatol*. 2020. https://doi.org/10.1016/j.jaad.2020.03.096.
5. Thompson BJ, Ravits M, Silvers DN. Clinical efficacy of short contact topical 5-fluorouracil in the treatment of keratoacanthomas: a retrospective analysis. *J Clin Aesthet Dermatol*. 2014;7(11):35-37.
6. Mascitti H, De Masson A, Brunet-Possenti F, et al. Successful treatment of generalized eruptive keratoacanthoma of Grzybowski with acitretin. *Dermatol Ther (Heidelb)*. 2019;9(2):383-388.
7. LaPresto L, Cranmer L, Morrison L, Erickson CP, Lewandrowski CC. A novel therapeutic combination approach for treating multiple vemurafenib-induced keratoacanthomas: systemic acitretin and intralesional fluorouracil. *JAMA Dermatol*. 2013;149(3):279-281.