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Controversies: Medical therapy for keratoacanthomas

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Controversies: 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 in this issue of the JAAD (*insert reference*) have done an excellent job of discussing the role of 5-fluorouracil (5FU) injections in primary treatment of selected patients and prevention of recurrence, but maintain that surgery remains the gold 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 where medical rather than surgical therapy represents the gold standard of treatment. Examples include KAs infiltrating into vital structures and widespread eruptive keratoacanthomas.

Keratoacanthomas can grow quickly and impinge upon vital structures including eyelids, the nose, lips and digits. Perineural invasion occurs with a wide variation in reported incidence but does not appear to affect outcome in most cases.^{1 2} Figure 1 demonstrates a patient who presented to Walter and E Dorinda Shelley with a giant keratoacanthoma infiltrating both upper and lower lips and well as the nasal filtrum. The patient was managed with psoriatic doses of

oral methotrexate with complete resolution of the lesion (Figure 2). While the cosmetic outcome is not perfect, it is amenable to surgical repair 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. It should also be noted that the majority of the linear scarring in this patient relates to the elliptical incisional biopsy needed to evaluate the lesion rather than the natural history of the lesion itself. In short, there are instances where surgery is associated with greater morbidity than medical therapy, and it is medical option that represents the gold standard.

Intralesional injection of methotrexate (MTX) has been used as an alternative to 5FU injections³ and is associated with less burning. I typically prescribe 2mg of folic acid daily for 1 week to reduce the risk of associated nausea when using MTX as an alternative to 5FU. Supplemental Figures A and B (<http://dx.doi.org/10.17632/6wpwmkmdt3.2>) demonstrate a patient with a large keratoacanthoma involving the digit. Such lesions commonly demonstrate perineural involvement and this patient had been scheduled for amputation. Prior to amputation, an enlightened hand surgeon consulted dermatology -- the lesion regressed entirely following intralesional MTX injection with sparing of the digit. I believe this patient would argue that medical therapy was the gold standard and superior to the surgical option of amputation.

Eruptive KAs (Figure 3) may be associated with an inherited genodermatosis, BRAF inhibition, or may occur sporadically on the extremities of older individuals. The old quip is that when one 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 following surgical excision. I have even seen patients who were referred to an oncologist and scheduled for conventional systemic chemotherapy for “metastatic squamous cell carcinoma” in this setting. It is far better to manage such patients with intralesional 5FU or MTX injection, topical 5FU cream

under Unna boot occlusion⁴, systemic acitretin⁵, or a combination⁶. I typically saucerize the largest lesions, infiltrate the base with a small amount of 5FU or MTX, apply a thick coat of 5FU cream and an Unna boot. The “chemoboot” is replaced weekly until all lesions are resolved. Typically, only one or two 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.

Figure Legends:

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

Figure 1: Resolution of giant KA following oral low-dose MTX (Image courtesy of E Dorinda Shelley. Reprinted with permission from *Cutis*.)

Figure 3: Sporadic eruptive keratoacanthomas on the leg. The lesions resolved completely with 5FU under unna boot occlusion.

Supplemental Figure A: Large keratoacanthoma in a patient scheduled for amputation of the digit (Courtesy of Omar Noor, Rutgers University, Robert Wood Johnson School of Medicine)

Supplemental Figure B: Complete resolution of large keratoacanthoma without the need for amputation of the digit (Courtesy of Omar Noor, Rutgers University, Robert Wood Johnson School of Medicine)

¹ Lapins NA, Helwig EB. Perineural Invasion by Keratoacanthoma. *Arch Dermatol* 1980;116(7):791-3.

² Godbolt AM, Sullivan JJ, Weedon D. Keratoacanthoma With Perineural Invasion: A Report of 40 Cases. *Australas J Dermatol* 2001; 42(3):168-71.

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Smith C, Srivastava D, Nijhawan RI. Intraleisional methotrexate for keratoacanthomas: a retrospective cohort study. *JAAD*, 2020. ePublished April 05, 2020DOI:<https://doi.org/10.1016/j.jaad.2020.03.096>

⁴ 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 Nov; 7(11): 35–37.

⁵ Mascitti H, De Masson A, Brunet-Possenti F, Bouaziz JD, Laly P, et al. Successful Treatment of Generalized Eruptive Keratoacanthoma of Grzybowski with Acitretin *Dermatol Ther (Heidelb)* 2019 Jun; 9(2): 383–388.

⁶ LaPresto L, Cranmer L, Morrison L, Erickson CP, Lewandrowski CC. A Novel Therapeutic Combination Approach for Treating Multiple Vemurafenib-Induced Keratoacanthomas: Systemic Acitretin and Intraleisional Fluorouracil. *JAMA Dermatol*. 2013 Mar; 149(3): 279–281



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Sharon Finch <sfinch@mdedge.com>

Sat 6/20/2020 9:20 AM

Forward

CAUTION: External

Hi Dirk,

I hope you and the family are doing well. Of course we grant permission.

Warm regards,

Sharon

Sharon Finch

SVP/Group Publisher

Cutis/Current Psychiatry

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On Sat, Jun 20, 2020 at 7:47 AM Elston, Dirk <elstond@musc.edu> wrote:

Melissa and Sharon,

I've been asked to write a counterpoint article for JAAD about medical therapy for keratoacanthomas and would like to use Cutis images from the 1980's (attached). Dorinda Shelley was kind enough to dig them out from Walter's files in their barn. Do I have permission to use the images in the manuscript? I will of course give credit to Cutis and the Shelleys.

Thanks,

Dirk

Omar Noor <noorom@gmail.com>
Sat 6/20/2020 8:32 AM

CAUTION: External

Hi Dr. Elston!

Of course you can use the photos, thank you for asking. Things are getting better here, but I fear a 2nd wave. I hope all is well with you and your family!!

Omar

On Jun 20, 2020, at 8:02 AM, Elston, Dirk <elstond@muscc.edu> wrote:

Omar,
Hope all is well in NY given all the current challenges. May I have permission to use the attached images in a JAAD article about medical treatment for KAs? I would, of course, give you credit for the images.

Thanks,

Dirk

<Picture2.tif>

<Picture3.tif>