

### Intralesional methotrexate for keratoacanthomas: A retrospective cohort study



*To the Editor:* Keratoacanthomas (KA), often classified as a subtype of squamous cell carcinoma, are classically characterized by rapid growth with pain or itching and potential spontaneous resolution.<sup>1,2</sup> Treatment is often surgical; however, alternate options are often sought. Successful use of intralesional (IL) agents such as methotrexate (MTX) (up to 88% resolution)<sup>3</sup> or 5-fluorouracil (up to 67% resolution)<sup>4</sup> has been reported for KAs, although in small cohorts. This institutional review board–approved study reports additional data on the efficacy of IL MTX for KAs.

In this single-center, retrospective cohort study, adult patients with histologic and/or clinical findings of KAs treated between October 2009 and February 2019 were identified by injectable drug (J-code) searches. When offered off-label IL MTX, patients were always informed of all possible treatment options. Baseline laboratory tests, if performed, consisted of a pretreatment basic metabolic panel to check creatinine based on the physician's concern for a patient's risk or history of renal disease. Patients who opted for IL MTX were all injected similarly at the base of their lesion with the syringe plunger pulled back before medication injection to ensure no intravascular injection. MTX (concentration of 25 mg/mL) was injected with the goal of lesion blanching with a volume proportional to the lesion size but a maximum volume of 1 mL per lesion per session. The goal was an injection every 2 to 4 weeks, with adjustments according to progress and preference. Patient and lesion data as well as treatment and response were recorded. Statistical analysis was done using a 2-sided *t* test with unequal variance and 2-sided Fisher's exact test.

Twenty-nine immunocompetent patients with 69 lesions were included. [Table I](#) lists demographic and medical history data. [Table II](#) lists characteristics and treatment of the lesions. Patients were generally older than 65 years, with female predominance. Interestingly, the skin cancer history predominance in this cohort was squamous cell carcinoma more than basal cell carcinoma. Lesions greater than 10 mm by largest diameter required significantly more total MTX ( $P < .001$ ) and longer duration of treatment ( $P = .02$ ) but similar numbers of total injections ( $P = .51$ ). No adverse reactions were reported after injection.

Four lesions were re-biopsied per patient request after IL MTX, and all showed only scar. Treatment

**Table I.** Patient (N = 29) characteristics

Characteristics	Values
Age, years, median (SD, range)	75 (9, 52-92)
Sex, n (%)	
Male	8 (28)
Female	21 (72)
Lesion multiplicity, n (%)	
Single lesion	18 (62)
Multiple lesions	11 (38)
Current smoker, n (%)	
Yes	4 (14)
No	25 (86)
Diabetes, n (%)	3 (10)
PVD, n (%)	5 (17)
IBD, n (%)	1 (3)
Transplant, n (%)	0 (0)
Immunosuppressant drug, n (%)	0 (0)
History of skin cancer, n (%)	
BCC	9 (31)
SCC	22 (76)
Melanoma	5 (17)
Unspecified	1 (3)
None	3 (10)

BCC, Basal cell carcinoma; IBD, inflammatory bowel disease; PVD, peripheral vascular disease; SCC, squamous cell carcinoma; SD, standard deviation.

success was 95.7% (66/69 lesions). This high response rate is likely due to specific patient and lesion selection (eg, lesions characteristically consistent with KAs and older patients with extremity lesions wishing to avoid surgery). We are more inclined to encourage definitive surgical management for KAs that occur in the head and neck areas.

Two of 69 lesions partially responded. Another biopsy-proven KA had no response to 2 IL MTX injections. There were no defining characteristics of these lesions compared with those successfully treated with IL MTX. When suspected KAs do not respond to intralesional treatment, it is critical to re-evaluate and consider alternative intervention.

This study shows the efficacy of off-label IL MTX for select KAs. Limitations include repeat office visits for injections and lack of histologic evaluation unless posttreatment re-biopsy is performed.

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**Table II.** KA lesion characteristics and treatment response

Characteristics	Values
Lesion location, n (%)	
Leg L	35 (51)
Leg R	27 (39)
Arm L	3 (4)
Arm R	4 (6)
Lesion size, mm, n (%)	
<6	10 (15)
6-10	21 (30)
11-20	20 (29)
>20	7 (10)
Not specified	11 (16)
Biopsy proven KA, n (%)	45 (65)
Total cumulative MTX over treatment course, mg, mean (SD)	39 (25)
Treatment response, n (%)	
Complete resolution	66 (96)
Partial resolution	2* (3)
No response	1 (1)
Additional treatment, n (%)	
Mohs surgery	1 (1)
ED&C	1 (1)
Topical 5-FU	1 (1)
Number of injections, mean (range)	2 (1-7)
Time course of injections, days, mean (range)	37 (0-245 <sup>†</sup> )
Lesion size compared to MTX amount	$P < .001$
≤10 mm, MTX in mg, mean (SD)	29 (18)
>10 mm, MTX in mg, mean (SD)	51 (25)
Lesion size compared to duration of treatment	$P = .02$
≤10 mm, mean days (SD)	24 (33)
>10 mm, mean days (SD)	56 (60)
Lesion size compared to average number of injections	$P = .51$
≤10 mm, mean (SD)	2.2 (1.2)
>10 mm, mean (SD)	2.6 (1.2)

5-FU, 5-fluorouracil; ED&C, Electrodesiccation and curettage; KA, keratoacanthoma; MTX, methotrexate; SD, standard deviation.

\*One biopsy-proven KA that only partially responded was previously treated with radiation at an outside facility, followed by 4 intralesional MTX injections with significant improvement and then subsequently treated with topical 5-FU with resolution. The other partially responding biopsy-proven KA lesion was treated with electrodesiccation and curettage after 2 injections per patient preference.

<sup>†</sup>The patient with a 245-day treatment course had 4 injections of this lesion and a long course because of sporadic appointment scheduling.

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#### An Internet-based survey study of patients with hidradenitis suppurativa: Use of the Internet for disease-related information



*To the Editor:* The prevalence of hidradenitis suppurativa (HS) has been estimated as high as 4%.<sup>1</sup> There is often a delay in diagnosis of nearly 7.2 years and another 2-year lag until initiation of adequate treatment.<sup>2,3</sup> The Internet can increase disease awareness and decrease delays in diagnosis if the appropriate information is available to patients. As a step toward this goal, we sought to determine what information patients with HS seek online, because this knowledge will allow the development of online resources that reflect their needs.

One advantage of the Internet is that it allows patients to connect and share recommendations, which has even led to the discovery of new treatments such as low-dose naltrexone for Hailey-Hailey disease.<sup>4,5</sup> A disadvantage is that there is no regulation of the sources, which can result in the spread of false—even harmful—information.

After institutional review board exemption from Wayne State University, a survey was developed and posted in the Reddit website's "Hidradenitis" forum and in the "Hidradenitis Suppurativa" Facebook group from April through May 2019 (Supplemental Figure S1; available via Mendeley at <https://doi.org/10.17632/8kk7xyk53m.1>). The final survey consisted of 21 questions related to HS, access and use of the Internet, and HS information-seeking behaviors.

Before diagnosis, 77.3% (109/141) of participants used online search engines (Google, Bing, Yahoo, etc) to learn about their symptoms (Fig 1 and 2). Among the undiagnosed population, 42.0% (55/131) of participants believed this information assisted in obtaining their diagnosis from a physician. Nearly half of respondents reported sharing advice online