Is the first-line treatment of keratoacanthomas surgical excision or injection of intralesional chemotherapy?

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Keratoacanthomas (KAs) are epidermal tumors that some physicians consider benign while others consider to be a type of squamous cell carcinoma.[1] KAs present as rapidly growing papules that develop into crateriform nodules with hyperkeratotic plugs. Although KAs can spontaneously involute, dermatologists typically treat them because of their uncertain behavior, potential for local tissue destruction, variable final size, and unpredictable resolution time.[1,2] Before treatment, a lesional biopsy should be performed to prevent misdiagnosis of KA as squamous cell carcinoma. KAs are generally treated with injections of intralesional chemotherapy, commonly methotrexate or 5-fluorouracil, and/or surgical excision.[1] Surgical excision of KAs is advantageous in many cases, but intralesional chemotherapy may offer a better alternative in others.

Abbreviations used:

KA: keratoacanthoma
MMS: Mohs micrographic surgery

INTRALESIONAL CHEMOTHERAPY

The resolution rates of KAs treated with intralesional methotrexate and 5-fluorouracil are 88% to 94% and 96% to 98%, respectively.[1-4] In one study, the clearance rate with intralesional methotrexate dropped to 57% in KAs greater than 2 cm^2. However, the KAs that did not completely resolve reduced in size.[2] No KA recurrences have been noted after treatment with intralesional 5-fluorouracil and methotrexate with follow-up as long as 24 and 91 months, respectively.[4] Table I shows the common dosing regimens of intralesional methotrexate and 5-fluorouracil. Multiple studies observed 50% to 70% improvement after 1 injection and resolution within 1 month of starting treatment.[3] It has been recommended that if the tumor enlarges or remains unchanged after 2 to 3 intralesional injections, surgical treatment should be performed. Despite the common use of intralesional chemotherapy for KAs, the US Food and Drug Administration considers this use to be off label.[4]

The local adverse effects of intralesional methotrexate and 5-fluororuacil are similar, but intralesional 5-fluororuacil is typically more painful than methotrexate (Table I).[4] Topical anesthetics and/or diluting the chemotherapy agent with 1% lidocaine with 1:100,000 epinephrine can help reduce the pain.[1,2] Using epinephrine causes vasoconstriction, decreasing diffusion of the chemotherapy agent.[2] A primary concern of intralesional chemotherapy is the immediate leakage of the medication, estimated to be 30% to 50%, between the keratinous plug and KA shoulder.[1]

SURGICAL EXCISION

Mohs micrographic surgery (MMS), standard surgical excision with 5-mm margins, and electrodesiccation and curettage are the surgical techniques frequently used to remove KAs. The resolution rate of KAs treated with standard surgical excision and MMS is approximately 100%.[2] The recurrence rates of KAs treated with standard surgical excision, MMS, and electrodesiccation and curettage have been shown to be approximately 0.9%, 0.8%, and 12.5%, respectively.[5] Surgery carries a risk of pain, scarring, infection, and functional and aesthetic deficits.[2]

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Table I. Comparison of intralesional methotrexate and 5-fluorouracil in the treatment of keratoacanthomas*

Intralesional chemotherapy	Concentration, mg/mL	Interval, wk	Individual injections, mL/KA	Average resolution time, wk	Resolution rate, %	Local adverse effects
Intralesional methotrexate	12.5 or 25	1-3	0.1-2.0	4.6	88-94	Erythema, crusting, ulceration, necrosis, pain
Intralesional 5-flourouracil	50	1	0.1-0.5	3.7	96-98	Erythema, crusting, ulceration, necrosis, pain

KA, Keratoacanthoma.
*Adapted from Kiss et al,[1] Moss et al,[2] Seger et al,[3] and Kirby and Miller.[4]

Table II. Factors other than resolution and recurrence rates to consider in selecting the final treatment option*

Factors	Intralesional chemotherapy	Surgical excision
Adverse effects	Local adverse effects: pain, erythema, crusting, ulceration, and necrosis	Pain, scarring, infection, and functional/aesthetic deficits
Patient variables	Recommended for patients who are at high risk of slow wound healing or surgical complications, want to avoid surgery, and/or present with KAs on cosmetically sensitive areas	Recommended for patients with low surgical risk factors and isolated lesions
Logistics and cost	Generally requires multiple office visits, which may be inconvenient and expensive for the patient KAs that do not resolve will likely shrink and become easier to excise.	Typically a 1-time, definitive procedure, which may be preferable and less expensive for the patient

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*Adapted from Kiss et al,[1] Moss et al,[2] Seger et al,[3] and Kirby and Miller.[4]

CONCLUSION

In conclusion, surgical excision is considered the criterion standard for treating KAs, but intralesional chemotherapy can be considered a first-line treatment option for select patients.[1,3] The final treatment decision will depend on several variables (Table II). Because of the lack of randomized controlled trials, it is difficult to recommend a treatment algorithm that applies to every patient. Based on our experience, we perform weekly injections of 50 mg/mL of 5-fluorouracil. If the KA does not improve after 2 injections, surgery is performed. Recurrent KAs are treated with MMS regardless of the site of involvement and prior treatment modality.

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