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## RESIDENT'S FORUM

# [Translated article] RF - Nonsurgical Treatment of Keratoacanthomas<sup>☆</sup>

## FR - Tratamiento no quirúrgico de los queratoacantomas

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### PALABRAS CLAVE

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5-Fluorouracilo

Keratoacanthoma (KA) is a skin tumor that, unlike classic cutaneous squamous cell carcinoma (SCC), grows rapidly and can subsequently partially or completely resolve. While some evidence supports its classification as a well differ-

entiated variant of SCC, this remains a topic of debate. Clinical differentiation from SCC can be difficult, but it is useful to distinguish one from the other, as there are non-surgical therapeutic options (Table 1) that may be useful for the treatment of KA, including intralesional infiltration of methotrexate (MTX) or 5-fluorouracil (5-FU), as well as topical application of imiquimod or 5-FU.<sup>1,2</sup> Other, less frequently used intralesional substances, for which less supporting data are available, include bleomycin, corticosteroids, and interferon alfa.<sup>3</sup>

Moss et al.<sup>4</sup> recently published the largest study comparing intralesional MTX with conventional surgery in patients with a clinical or histological diagnosis of KA (n=136; 157 tumors). In each case, the treatment decision was reached following consultation between the physician and the patient. In the 54 patients (n=73) for whom intralesional MTX was indicated, a variable volume of 0.075-1 mL (depending on tumor size) was injected into the tumor base at a concentration of 12.5 mg/mL (25 mg/mL MTX diluted 50% with 1% lidocaine and 1:100 000 adrenaline). Doses were administered every 2-4 weeks. Complete resolution after 1 to 4 infiltrations (mean, 2.1) was observed in 88% (64 of 73) of KAs. Clinical cure was confirmed between 6 and 8 weeks after the last infiltration. The 9 patients who did not respond to intralesional MTX (8 KA lesions decreased in size and 1 remained unchanged) presented solitary KAs that were treated surgically, without complications. No moderate-to-severe adverse effects were observed in any of the patients

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**Table 1** Nonsurgical Alternatives for the Management of Keratoacanthoma.<sup>a</sup>

Drug	Route of administration	Dose	Interval	Duration	Adverse effects
Methotrexate	Intralesional	12.5 mg/mL (0.075-1 mL)	1-4 weeks	1-4 weeks	Moderate pain at moment of injection Pancytopenia <sup>b</sup>
5-Fluorouracil	Topical	5% ointment	1-3 times per day	1-8 wk	Mild skin irritation Acute pruritus and contact dermatitis
	Intralesional	15 mg	1 wk	3-4 wk	Discomfort at moment of injection Focal irritation and necrosis Hypopigmentation, purulent exudate Erythema, edema, and lymphedema Erythema and crusting
Imiquimod	Topical	5% cream	1-3 times per week	3-11 wk	Erythema, pigmentation
Bleomycin <sup>c</sup>	Intralesional	0.2-0.4 mg	1 wk	2-6 wk	Local pain
Interferon alfa <sup>c</sup>	Intralesional	3 MUI	1 wk	5-7 wk	Neutropenia Urticaria Flu-like symptoms
Corticosteroids <sup>c</sup>	Intralesional	50 mg HC	1 wk	2 wk	Hypopigmentation

Abbreviations: HC, hydrocortisone; MUI, million international units.

<sup>a</sup> We always recommend histological confirmation before indicating nonsurgical treatment, as it can be difficult to clinically differentiate keratoacanthoma from cutaneous squamous cell carcinoma.

<sup>b</sup> Despite the fact that no moderate or serious adverse effects have been recorded in the majority of patients, pancytopenia after treatment with intralesional methotrexate has been described in 2 patients with chronic kidney disease. It is therefore recommended to perform laboratory tests before and after drug infiltration.

<sup>c</sup> There is limited evidence supporting the efficacy of these drugs for the treatment of keratoacanthoma.

treated with intralesional MTX. Mohs micrographic surgery was used for all of the 84 surgically-treated tumors, without recurrences or surgical complications. In an Italian series of 11 elderly patients with KA, mainly affecting the head and hands, weekly intralesional MTX infusions (median, 5.3; range, 4-8) resulted in complete resolution in all cases, without systemic adverse effects or recurrences after 6-9 months of follow-up.<sup>5</sup>

A 2019 systematic review of nonsurgically-treated KA (n=184), not including the series by Moss et al.,<sup>4</sup> found no significant differences in the rate of resolution between topical and intralesional treatments (92% and 100%, respectively), but reported a faster response for intralesional 5-FU versus intralesional MTX (3.7 vs 4.6 wk, which may not constitute a clinically significant difference) and for topical 5-FU versus topical imiquimod (3.8 vs 7.6 wk).<sup>1</sup> Similar findings were reported in another recent review, with a 94% cure rate and no adverse effects of note.<sup>3</sup>

Spanish authors evaluated intralesional MTX as neoadjuvant therapy prior to KA surgery, and concluded that it is a well-tolerated measure that precludes the need for aggressive surgeries in facial or acral areas in elderly patients.<sup>2</sup>

Because spontaneous resolution of KA can take up to 1 year, or not occur at all, most authors recommend tar-

geted treatment. Nonsurgical techniques (infiltrations and topical treatments) can be valid alternatives for KA located in complex areas (facial or acral) or in elderly patients.

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