Comment on "Intralesional methotrexate for keratoacanthomas: A retrospective cohort study"

To the Editor: We read with particular interest the article recently published by Smith et al.[1] In this article, Smith et al conducted a study of 29 patients with 69 cutaneous lesions defined as keratoacanthomas (KAs) that were treated with a variable dose range of intralesional methotrexate (il-MTX), achieving a complete response in a 97.6% of cases.[1]

Surprisingly, all tumors were located on the arms and legs, with not one arising on the face. In addition, 51 of 69 tumors (73.9%) presented as multiple lesions in 11 patients, for whom an approximate average of 4.6 KAs per patient could be estimated. Given that KA appears preferentially as a solitary lesion on sun-exposed face areas,[2] multiple lesions limited to limbs in a cohort of 29 nonconsecutive patients suggests that a selection bias cannot be ruled out.

Recently, the term *eruptive squamous atypia* (ESA) was introduced by the Brigham and Women's Hospital research group, leading to the ability to distinguish between KA and those synchronous multiple hyperkeratotic lesions developing on the extremities, historically known as *eruptive keratoacanthomas*.[3]

According to this publication, we believe that many of the tumors treated by Smith et al[1] could meet these criteria and may have been misdiagnosed. We consider that this likely situation, as well as the lack of systematic histopathologic evaluation of the tumors, could have notoriously overestimated the real efficacy of il-MTX in KA.

Similar conclusions can be deduced from other studies. Moss et al[4] reported a 88% overall rate of tumor clearance. Nonetheless, 100% of multiple lesions (all located on extremities) resolved with il-MTX, whereas only 79% of solitary tumors showed a complete response.

Indeed, the high effectiveness rate observed in these 2 studies supports the investigation by Que et al,[3] who considered KA and eruptive squamous atypia as different entities and remarked on the importance of careful management.

Furthermore, Smith et al[1] stated that they were more inclined to encourage definitive surgical management for KAs that occur in head and neck areas. Nevertheless, preliminary data about il-MTX treatment of face KAs is available, even in cases of squamous cell carcinomas as neoadjuvant therapy to surgery.[5] Although we absolutely agree on the surgical approach to a solitary crateriform lesion on the face with no response to il-MTX, we believe that its use can be taken into consideration depending on each individual patient and should not be relegated in all cases when KA arises on the head or neck.

Finally, we would like to gratefully acknowledge the authors for this contribution, which enhances understanding of KA management. However, controlled studies with a specific regimen and appropriate selection criteria are required.

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