Multiple reactive keratoacanthomas treated with zinc oxide wraps and intralesional corticosteroids

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INTRODUCTION
Keratoacanthoma (KA), a neoplasm of epidermal cells from the hair follicle unit, is often present on chronic sun-exposed skin. Many facets of this neoplasm are controversial, including its epidemiology, etiology, and biologic behavior, including malignant potential and recommendations for treatment. This case presents a treatment option for multiple reactive KAs that is both conservative and noninvasive.

CASE REPORT
An uninsured 62-year-old white woman with a history of peripheral neuropathy was referred for numerous tender lesions on her bilateral legs. On examination of her lower extremities, there were numerous discrete hyperkeratotic papules, some areas coalescing into plaques, with crusting and erosions distal to her knees, in the setting of lower leg edema (Fig 1). The lesions first appeared more than 1 year before presentation when a bump appeared on her left leg after local trauma. Over the subsequent weeks to months, multiple similarly painful and itchy bumps appeared. A shave biopsy found a crateriform keratinocytic proliferation with epidermal hyperplasia and a central keratin plug, consistent with a keratoacanthoma (Fig 2). Periodic acid-Schiff and FITE stains were negative for microbial elements; however, a tissue culture isolated the mold Curvularia species. Given the histopathology in the context of trauma, the favored diagnosis was multiple, reactive KAs. She had tried and not responded to multiple therapies prescribed by outside physicians, including systemic antibiotics, topical steroids, and topical 5-fluorouracil. The patient, who had been applying essential oils to her legs, desired as natural of an approach as possible, and she declined any systemic medications offered such as acitretin and methotrexate. Because of the concern that many of these lesions were inflammation driven and self-induced from scratching given her reported pruritus, she was instructed to stop all previous topical agents. Intraleisonal injection of triamcinolone 40 mg/mL was prescribed for select tender lesions followed by zinc oxide wraps (Unna boots) to provide barrier protection, reduce inflammation, and minimize her lower extremity edema. Itraconazole was prescribed for the isolated curvularia species; however, she never took more than a few days of it, as she preferred to avoid systemic medications.

After 2 weeks of Unna boot application, consisting of zinc oxide wrap followed by kerlix gauze then self-adherent wrap, there was notable flattening of her lesions with less edema, pruritus, and pain in her legs (Fig 3). After 10 weeks of almost weekly repeated Unna boot application and 2 courses of intraleisonal steroid injections into select lesions, all but 2 of her initial 30+ lesions had completely resolved. At 15 weeks, Unna boots were discontinued on her right leg, as the 2 remaining lesions were present on the left leg only. After 21 weeks of Unna boots to her left leg, 1 lesion persisted. Her final KA resistant to therapy was removed with electrodessication and curettage at 21 weeks (Fig 4). In total, she...
completed 23 weeks of Unna boot wraps on her left leg and 15 weeks on her right, with approximately once-per-month injections of intralesional triamcinolone to symptomatic lesions with no evidence of recurrence 4 months after Unna boot therapy.

**DISCUSSION**

KAs usually arise as a solitary lesion and less commonly in multiples. Multiple KAs can either be classified as sporadic or familial. It is important to distinguish multiple eruptive KAs that arise as part of a familial genetic syndrome, such as Witten and Zak, Ferguson-Smith, and Grzybowski, from multiple reactive KAs, which typically arise in response to an external insult. Many etiologies for multiple reactive KAs have been described, such as trauma, inflammation, and iatrogenic causes secondary to surgery or topical drugs. Multiple reactive KAs can be difficult to treat, with patients often going through repeated courses of relapse and remission. There are many documented cases of recurrence of this neoplasm in the surgical margins after excision or skin grafting and even recurrences to areas of intralesional injections and radiation. Koebnerization after trauma may predispose patients to KA development secondary to increased vessel formation and epidermal proliferation.

Solitary KAs are often surgically excised because of their controversial malignant potential and association with squamous cell carcinomas. Multiple
KAs are often treated with systemic retinoids, either alone or in combination with surgery or other types of intralesional chemotherapy. Intralesional corticosteroids were used to treat multiple KAs often historically; however, intralesional chemotherapies such as methotrexate and fluorouracil are now more commonly used. Many advantages to using intralesional steroids include reduced inflammation, pain, scarring, and limited systemic side effects. Many KAs in this patient were thought to have developed from repetitive scratching/koebnerization, and intralesional steroids helped to reduce inflammation and allow for self-resolution of the lesion.

To our knowledge, there is only one prior report on the successful use of zinc oxide wraps to treat multiple reactive KAs over 18 months. Topical zinc oxide has antiseptic, anti-inflammatory, astringent, and protective qualities. It also aids in removal of wound debris and promotion of epithelialization in wound healing. The anti-inflammatory mechanisms of zinc oxide are theorized to be from its ability to prevent formation of nitric oxide and oxidation of sulphhydryl groups. Unna boots, which our patient learned to self-apply at home, also serve as a compression device to reduce swelling and aid in healing and as a physical barrier to prevent additional trauma.
We report a case of multiple reactive KAs that responded dramatically to a noninvasive, conservative, and nontraditional treatment regimen of serial zinc oxide wraps and intralesional steroids, with a total treatment duration of less than 6 months. This regimen allowed all but 2 of her numerous KAs to resolve within 10 weeks of treatment and her quality of life to be greatly improved. We propose that zinc oxide wraps and intralesional corticosteroids be considered in cases of multiple reactive KAs or KAs that arise secondary to trauma because of the ability to reduce inflammation and swelling, prevent further trauma, and allow for self-involution of the lesions.

REFERENCES
1. Kwiek B, Schwartz RA. Keratoacanthoma (KA): An update and review. J Am Acad Dermatol. 2016;74(6):1220-1233.
2. Schwartz RA. Keratoacanthoma: a clinico-pathologic enigma. Dermatol Surg. 2004;30(2 Pt 2):326-333. discussion 333.
3. Nofal A, Nofal E. Multiple eruptive keratoacanthomas: a confusing term? J Dtsch Dermatol Ges 2013;11(8):756.
4. Hsu S, Hill AN, Conrad N, Wood AC, Reed JA. Reactive multiple keratoacanthoma in a patient with chronic renal insufficiency. Br J Dermatol. 2003;148(6):1270-1271.
5. Sanders S, Busam KJ, Halpern AC, Nehal KS. Intralesional corticosteroid treatment of multiple eruptive keratoacanthomas: case report and review of a controversial therapy. Dermatol Surg. 2002;28(10):954-958.
6. Hadley JC, Tristani-Firouzi P, Florell SF, Bowen GM, Hadley ML. Case series of multiple recurrent reactive keratoacanthomas developing at surgical margins. Dermatol Surg. 2009;35(12):2019-2024.
7. Lee S, Coutts I, Ryan A, Stavrakoglou A. Keratoacanthoma formation after skin grafting: A brief report and pathophysiological hypothesis. Australas J Dermatol. 2017;58(3):e117-e119.
8. Zhu LY, Likhari SS, Stebbins WG. A case of multiple large reactive keratoacanthomas treated with serial zinc oxide wraps. Dermatol Surg. 2015;41(6):750-753.
9. Lansdown AB, Mirastschijski U, Stubbs N, Scanlon E, Agren MS. Zinc in wound healing: theoretical, experimental, and clinical aspects. Wound Repair Regen. 2007;15(1):2-16.