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THERAPEUTIC HOTLINE: LETTERS

Classic Kaposi's sarcoma treated with topical 0.5% timolol gel

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To the editor,

Kaposi's sarcoma (KS) is an angioproliferative disorder closely associated with human herpesvirus type 8. Classic KS is found mainly in elderly males, with lesions beginning slowly and insidiously on the distal lower extremities and occasionally on the hands. Although the disease is very rarely responsible for the death of the patient, there might be complications such as ulceration, bleeding and pain in nodules on pressure areas requiring treatment (1). To date, a uniformly effective and low-risk treatment for KS has not been found, so therapeutic recommendations must be individualized. Topical treatment would be ideal for patients with limited disease confined to the skin, since it may satisfactorily slow progression of classic KS for several years with lower risks of systemic side effects. In this way, some topical agents have been used with various results, including 5% imiquimod cream (2), 0.5% rapamycin ointment (3), 0.1% alitretinoin gel (4) and very recently, 0.5% timolol maleate solution (5). We report here two cases of classic KS successfully treated with topical timolol. We used 0.5% timolol gel, applied twice daily. To our knowledge, this is the second report of classic KS treated with topical timolol.

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Case 1

An 89-year-old man with hypertension, was referred for evaluation because an 8-month history of asymptomatic purplish macules and nodules on the medial aspect of the toes (FIG. 1A). After a punch biopsy confirmed the diagnosis of KS, we initiated treatment with 0.5% timolol gel. The lesions decreased in size and volume gradually, and a complete clinical response was achieved 12 weeks from baseline (FIG. 1B). The treatment was stopped, and no recurrence has been detected after 5 months.

Case 2

A healthy 83-year-old man, presented with a slow-growing crusty reddish nodule on the medial aspect of his finger, which had recently started bleeding (FIG. 2A). The B-mode ultrasound imaging showed an ill-defined, hypoechogenic nodule involving the dermis and upper subcutaneous tissue, with prominent lesional blood flow on color Doppler ultrasound (FIG. 3A). The diagnosis of KS was confirmed histologically and we initiated

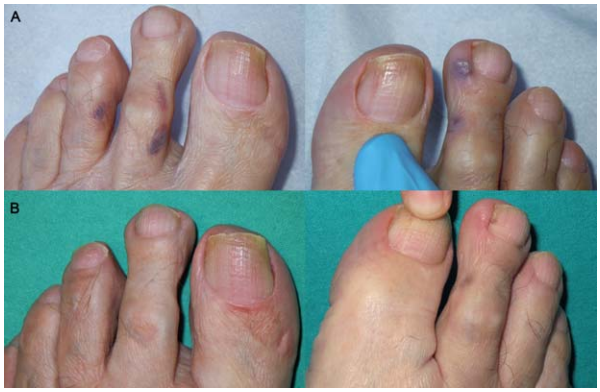

FIG. 1. (A) Before treatment. Purplish macules and nodules on the medial aspect of the toes. (B) After 12 weeks of treatment.

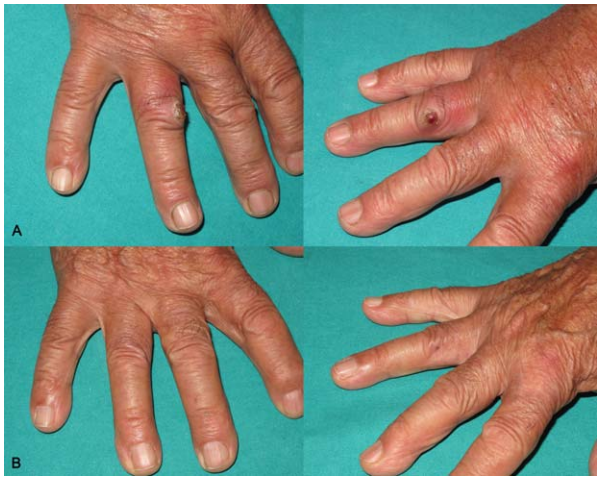

FIG. 2. (A) Before treatment. Crusty reddish nodule on the medial aspect of the finger. (B). After 18 weeks of treatment.

treatment with 0.5% timolol gel. After 18 weeks, only a milimetric brownish macule remained (FIG. 2B) with no evidence of increased vascularization in color Doppler (FIG. 3B), so we stopped the treatment. After 4 months of follow-up, there is no evidence of regrowth.

Timolol gel is a topical nonselective beta-blocker that has emerged as an effective treatment for superficial infantile haemangiomas (6). The effects of beta-blockers on infantile haemangiomas were discovered by chance, and although it is not completely understood, three pharmacodynamic characteristics of beta-blockers have been hypothesized as possible mechanisms of action in this condition, including vasoconstriction, inhibition of angiogenesis, and induction of apoptosis (7). In a recent study, Chisholm et al. (8) found strong expression of beta-adrenergic receptors in up to 75% of KS, providing a molecular basis that could explain the efficacy of timolol in treating KS, as suggested Meseguer-Yebra et al. (5). The main advantages of topical timolol are cost, ease of administration and, most important, minimal risk of drug-related adverse events. In our patients, the treatment was well tolerated and no systemic symptoms or skin-related adverse events were noted. Thus, we suggest 0.5% timolol gel could be an alternative for treatment of localized classic KS, since it appears to be effective and safe when applied topically on cutaneous KS. In our experience, basing the duration of treatment on clinical and sonographic evolution, a minimum of 12 weeks of treatment was required. The use of skin ultrasound imaging provides additional information on the structural and vascular characteristics of this angioproliferative disorder, which helps to monitor treatment.

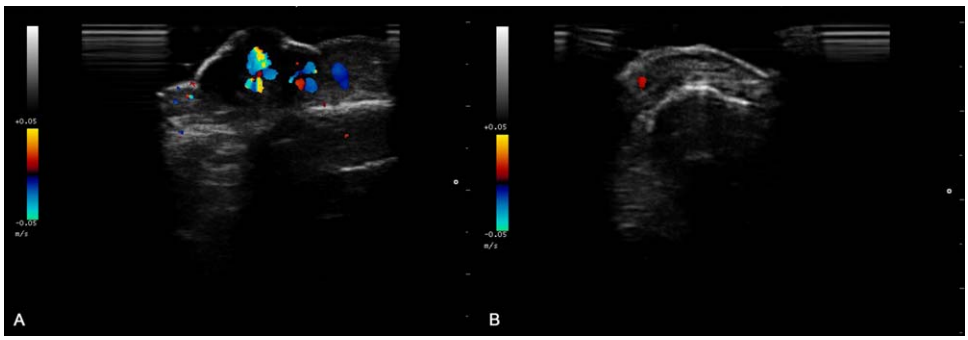

FIG. 3. Color Doppler ultrasound imaging. (A) Before treatment. Increased blood flow within the lesion. (B) After treatment. No evidence of increased vascularization.

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