



# Successful treatment of nodular human immunodeficiency virus–associated Kaposi sarcoma of the foot utilizing combination intralesional bleomycin and cryotherapy

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## INTRODUCTION

Kaposi sarcoma (KS) is a malignancy of endothelial cells caused by human herpesvirus 8, leading to an angioproliferative disorder that affects the skin and internal organs. KS is associated with immunosuppression, and people with advanced human immunodeficiency virus (HIV) have a several thousand-fold increased risk of acquiring KS.<sup>1</sup> A wide range of treatments have been attempted, but a single optimal therapy is yet to be identified.<sup>1</sup>

Intralesional chemotherapy is among the established treatments for KS; however, most reports focus on vinca alkaloid agents.<sup>2</sup> Bleomycin has been documented as an effective intravenous option, but intralesional bleomycin remains a rarely reported therapy.<sup>2,3</sup>

We report a case demonstrating the notable efficacy of intralesional bleomycin with combination cryotherapy for HIV-associated KS of the right foot.

## CASE REPORT

A 43-year-old, HIV-positive, Caucasian male, previously on combination antiretroviral therapy (cART), including elvitegravir, cobicistat, emtricitabine, and tenofovir, from 2005 to 2011 presented in January 2018 with numerous, tender lesions on his right foot, progressive for several months and impairing his ability to walk. He had been diagnosed with biopsy-proven KS in 2013, 2 years after cART had been discontinued. Since that time, cART was restarted, but without resolution of his KS. Workup for systemic

### Abbreviations used:

cART: combined antiretroviral therapy  
HIV: human immunodeficiency virus  
KS: Kaposi sarcoma

involvement was negative. Skin biopsy reconfirmed KS and palliative external beam radiation therapy was initiated. After 2 weeks, the radiation was discontinued due to inefficacy and replaced with intravenous doxorubicin. Despite 3 cycles of chemotherapy, new lesions continued to form. Topical imiquimod 5% cream 3 times weekly was added for 12 weeks. While no new lesions formed on this treatment regimen, existing lesions did not improve and ambulation remained painful, requiring a surgical boot.

Six months later, after 7 cycles of intravenous doxorubicin with adjuvant topical imiquimod, the patient was referred to the dermatology for exploration of alternative therapy. At this time, the examination revealed numerous violaceous papules coalescing into a 3 × 2 cm nodular plaque on the dorsal right second toe (Fig 1, A), a 1.5 cm nodule on the plantar R2 toe, and numerous papules on the dorsal and plantar foot associated with significant lower extremity edema (Fig 1, B). Inguinal lymphadenopathy was not present. The decision was made to initiate a trial of intralesional bleomycin (1.5 U/mL) into the affected areas in combination with cryotherapy, with the intent of rapidly restoring the quality of life. Other therapies were discontinued.

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**Fig 1.** KS lesions prior to treatment with intralesional bleomycin showing large nodules and plaques on the dorsal (**A**) and plantar (**B**) aspects of the right foot. KS, Kaposi sarcoma.

In the first treatment, 0.7 mL bleomycin was injected into the plaque on the R2 toe along with cryotherapy with liquid nitrogen administered in 2 freeze-thaw cycles. Within 3 weeks, improvement in lesion size was already noted. At all subsequent visits every 3–4 weeks, approximately 1.2 mL bleomycin was injected into the largest lesion on the R2 toe and 0.7 mL bleomycin was injected into the smaller nodule on the plantar aspect, along with cryotherapy. Cryotherapy alone was performed on the smaller surrounding papules of the dorsal and plantar aspects. The highest total volume of bleomycin injected at any one visit was 1.9 mL. At follow-up 6 months after starting treatment, significant improvement was noted of the right foot with complete flattening of the previous nodules and resolution of his lower extremity edema. As a result, intralesional bleomycin was discontinued. The patient transitioned from wearing a surgical boot to a normal shoe without pain. One year after beginning treatment with intralesional bleomycin, examination revealed continued resolution of skin lesions, edema, and discomfort (Fig 2, A and B).

## DISCUSSION

Treatments for KS can be categorized as topical therapies, physical agents, intralesional chemotherapy, and systemic treatments. Topical therapies include imiquimod cream<sup>4</sup> and 9-cis-retinoid acid (alitretinoin gel 0.1%).<sup>5,6</sup> Physical agents include radiotherapy, cryotherapy, and laser.<sup>7</sup> Surgical excision is another option, but it is limited to superficial,

small lesions and carries a high recurrence rate.<sup>7</sup> Systemic treatments are utilized to control disease and reduce symptoms with the goal of improving the quality of life. Reported agents include pegylated liposomal doxorubicin, paclitaxel, vinblastine, etoposide, bleomycin, interferon alpha-2a/2b, pomalidomide, and bevacizumab.<sup>7</sup> Other reported alternative treatments include sodium tetradecyl sulfate, topical timolol, matrix metalloprotease inhibitor (6-demethyl)-6-deoxy-4-dedimethylamino tetracycline, interleukin-12, imatinib, liposomal tretinoin, nivolumab, pembrolizumab, sorafenib, and thalidomide, but most have potentially serious side effects and lack sufficient supportive literature to become routine options.<sup>6</sup>

Intralesional chemotherapy has focused on vinblastine and vincristine, with reported response rates of >70%,<sup>7,8</sup> but these agents are not used commonly within dermatology. While bleomycin has been studied in this context, its use as an independent agent for KS is less common. Intralesional bleomycin was first described for this purpose in the 1980s, including the 1984 prospective study by Brambilla et al,<sup>9</sup> which documented 80% complete regression among 93 KS nodules and partial regression of the remaining 20%, using 0.1 mg vincristine or bleomycin per site. Poignonec et al<sup>3</sup> isolated the use of intralesional bleomycin for HIV-associated KS in 1995, showing a complete or partial response rate of 87% among 134 macular and nodular lesions treated with a median dose of 1.5 mg bleomycin per lesion. Side effects included



**Fig 2.** KS lesions after treatment with intralesional bleomycin 1 year later, showing resolution of the nodules and edema of the dorsal (A) and plantar (B) aspects of the right foot. KS, Kaposi sarcoma.

erythema, crusting, and hyperpigmentation and hypopigmentation. A 17% 3-year recurrence rate led the investigators to conclude that intralesional bleomycin may be useful in HIV-associated KS.

In our case, the patient's lesions had not been responsive to any of the typical HIV-associated KS therapies, including cART, systemic doxorubicin, and typical imiquimod, and he was not a good candidate for surgical excision or radiation therapy. With 6 months of intralesional bleomycin treatment, the KS lesions resolved and the patient regained his ability to perform functions of daily living. Given the paucity of literature documenting the successful use of intralesional bleomycin for the treatment of KS, this case adds valuable support for the use of this intralesional agent as a treatment option for HIV-associated KS. The addition of cryotherapy, which has demonstrated success as an isolated agent, likely contributed to the efficacy, lending support for this combination.<sup>7</sup> Given that intralesional bleomycin is a readily available agent that is used commonly in the outpatient dermatologic clinic setting for the treatment of verrucae, we argue that it should be considered a routine therapeutic option for cutaneous KS.

#### Conflicts of interest

None disclosed.

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