

BRIEF ARTICLES

The Successful Treatment of Multiple Cutaneous Malignancies with HPV Vaccination: Case ReportSolomon Geizhals BA¹, Mark G Lebwohl MD²¹SUNY Downstate Medical School, Brooklyn, NY²Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY

ABSTRACT

An elderly, immunocompetent patient presented multiple invasive squamous cell carcinomas of the keratoacanthoma subtype superimposed on a psoriatic plaque. After failing initial treatment with oral acitretin, alternative therapies were considered. Due to the patient's advanced age, location of the tumors and extensive tumor burden, invasive therapy was deemed impractical. After careful consideration, the more novel approach of injecting the 9-valent HPV vaccine was performed. Ten months after the first dose, the patient's skin displayed neither clinical or histologic evidence of any residual cancer. We believe that this is the second reported case of the 9-valent HPV vaccine successfully treating non-melanoma cutaneous malignancies.

CASE REPORT

An immunocompetent 84-year-old woman presented to a university-based outpatient dermatology clinic with more than 20 dome-shaped crusted nodules that were superimposed on a large, sharply demarcated erythematous plaque of psoriasis on her right leg (Figure 1A). Histopathologic examination of one of the nodules revealed an invasive squamous cell carcinoma (SCC) of the keratoacanthoma variant. Considering the patient's advanced age, location of the tumors and extensive tumor burden, invasive therapy was deemed unfeasible and a different therapeutic approach was warranted. Initially, oral acitretin 25 mg/day was prescribed to treat both the psoriasis¹ and the multiple keratoacanthomas.² After 3 months of

treatment, the tumors had all clinically resolved and the underlying psoriatic plaque nearly gone. However, due to complaints of increased skin-dryness, cheilitis, and some mild hair loss, the acitretin dosage was decreased to 10 mg/every other day with concurrent betamethasone dipropionate 0.05% ointment twice daily for 4 weeks and then twice per week after that. Unfortunately, 5 months later, there was a recurrence of multiple histopathologically-confirmed keratoacanthomas. After the patient declined increasing the acitretin dosage or any systemic therapy, she was treated off-label with vaccine administration. She was treated twice intramuscularly and three times intralesionally with the 9-valent HPV vaccine (0.5 mL each time) from September 12, 2018 through July 22, 2019. Clinical improvement was observed after two injections of the 9-valent HPV vaccine

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with reduction in tumor size and number (Figure 1B) after each injection. Ten months after the first dose, there was no clinical or histologic evidence of residual SCC. On examination, there were small violaceous discolored patches and scars on her right leg at sites corresponding to previous tumors (Figure 1C).

Figure 1. Clinical image of the right calf of an 84-year-old woman. Complete tumor regression was observed 10 months after the first dose of vaccine.

A. Prior to any injections



B. Three-months after 2 sets of injections.



C. Ten months after first injection.



DISCUSSION

Standard of care for non-melanoma skin cancers generally entails excision of the cutaneous malignancy, with limited alternatives. Those with multiple lesions or poor surgical candidates are left with few options for appropriate therapy. However, recent evidence suggests that the human papillomavirus (HPV), specifically the β -HPV subtypes types 5, 8, 15, 17, 20, 24, 36, and 38, contributes to the pathogenesis of SCC.³⁻⁴ Current evidence suggests that these β -HPV types play a role at an early stage of skin carcinogenesis, but are not required for the viability and maintenance of the malignant cell after development of the skin tumor.⁵ Regardless of the exact pathogenesis, the growing evidence showing the association between SCC prevalence and HPV infection can potentially help create new therapeutic avenues in reducing cutaneous malignancy prevalence.⁶ The 9-valent HPV vaccine is approved by the US Food and Drug Administration to prevent genital warts and anogenital cancer caused by HPV infection.⁷ It provides coverage only against the sexually transmitted α -HPVs, essential etiological variants in cervical, anal, penile,

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vaginal, vulvar, and some oropharyngeal cancers, but not against β -HPV types.⁶⁻⁷

Although the β -HPV subtype has been viewed as the main culprit in cutaneous malignancy pathogenesis, nevertheless, some patients that received the more limited quadrivalent vaccine reduced new SCC development in immunocompetent patients without known HPV infection.⁸ Another recent study reported the complete regression of multiple cutaneous basaloid squamous cell carcinomas in a 90-year-old female following both intratumoral and intramuscular injections of the 9-valent HPV vaccine (Gardasil-9; Merck & Co Inc).⁹ The mechanism of action is unclear; either due to an activation of innate immunity in response to the aluminum adjuvant in the vaccine,¹⁰ or more likely, to the contributing viral component.¹¹

Most keratoacanthomas are self-resolving benign epidermal lesions, but are generally considered a well-differentiated variant of SCC.² Moreover, it has been posited that a keratoacanthoma may represent a midpoint between a viral wart and invasive SCC, hence its propensity for spontaneous regression.⁴ Hence, since our patient continued to present with persistent keratoacanthomas after acitretin treatment and declined systemic therapy, this led to the consideration of the use of off-label treatments. The data supporting the use of intratumoral vaccine injections in eliciting immune responses capable of eradicating tumor cells¹² coupled with the evidence showing a strong relationship between HPV and non-melanotic skin cancers led us to treat and now report a 2nd case in which a patient's multiple cutaneous malignancies were successfully treated with the HPV vaccine.

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