Editorial

The human papillomavirus vaccine: a potentially novel treatment for basaloid squamous cell carcinoma

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In the United States, 42.5% of patients ages 18–59 years who sought treatment for genital infections throughout 2013–2014 were infected with any type of human papillomavirus (HPV) (1). The HPV affects millions of reproductive-age adults in the United States and countless more throughout the world. In 2016, the U.S. FDA released a 9-valent HPV vaccine, commonly known as Gardasil-9, with intended uses in preventing the contraction of HPV and development of HPV-related diseases (2). However, new research suggests that this vaccine may have other clinically significant treatment applications. A recent study published by Nichols *et al.* in *JAMA Dermatology* entitled "Combined systemic and intratumoral administration of human papillomavirus vaccine to treat multiple cutaneous basaloid squamous cell carcinomas", which proposes the 9-valent HPV vaccine may be able to treat basaloid squamous cell carcinomas (bSCCs) (3). This novel finding has the potential to positively affect not only the millions of people at risk for contracting HPV but also millions of patients suffering from basal and squamous cell carcinomas, BCCs and SCCs, respectively.

This report details the treatment of one 90-year-old female patient that sought treatment for "numerous large, nontender, exophytic tumors on her right leg" at a private dermatologist. Her tumors were confirmed to be bSCCs through histological examination. To assess whether the 9-valent HPV vaccine could be used as a treatment for bSCCs, the vaccine was administered intramuscularly in two doses over 6 weeks, followed by injection of the largest tumors 3 weeks after the second intramuscular injection. Intratumoral injection with the 9-valent HPV vaccine was repeated three times over eight months. A reduction in tumor size and number were observed after the second intratumoral injection. Complete remission was achieved 11 months after the first intratumoral injection, verified by histological assessment. The patient remained in remission through her final follow-up 24 months after the first intratumoral injection. However, histological examination did reveal that the patient had "mild cellular atypia of basal keratinocytes and hyperkeratosis" where one of the larger tumors had previously been (3). Aside from this, the patient exhibited minimal scarring with minimal additional side effects. These findings suggest the 9-valent HPV vaccine may be useful in treating bSCCs as well as preventing the contraction of HPV and HPV-derived conditions.

If the 9-valent HPV vaccine is approved by the FDA for treatment of bSCCs, there could be countless benefits to patients suffering from this type of skin cancer. The most obvious advantage is a reduced reliance on surgical intervention, chemotherapy, and radiation as treatments for bSCCs. Currently, the most effective treatment for basal cell carcinomas and squamous cell carcinomas is the Mohs surgery. Though the Mohs surgery is relatively safe, complications are possible. In a study of 1,343 patients, Cook *et al.* found major complications arise in approximately 1.64% of cases. Major complications of the Mohs surgery include "postoperative hemorrhage, hematoma formation, wound dehiscence, wound infection, flap necrosis, and skin

graft necrosis" (4). Nichols *et al.* reported that patients who received the quadrivalent HPV vaccine for the treatment of BCCs and SCCs saw a marked reduction in tumor growth over one year and suffered no adverse effects from the treatment (5). Though the vaccine used in the study above is quadrivalent, unlike the paper for which this editorial is written in which a 9-valent vaccine was administered, these findings do lend supporting evidence for a role of HPV in tumor suppression of bSCCs.

The association between HPV infection and development of cervical cancer is well described. Of the more than 100 types of HPV, two are known to cause approximately 70% of all cervical cancer cases, types 16 and 18. Since HPV is the most common sexually transmitted disease worldwide, cervical cancer has, likewise, ascended to be recognized as one of the most common cancers affecting women (6). Furthermore, according to the American Cancer Society, 90% of cervical cancers are squamous cell carcinomas of the cervix, suggesting there may be a link between a therapeutic HPV vaccine having applications in treating both cervical and noncervical SCCs. However, the association between HPV and noncervical cancers, such as cutaneous squamous cell carcinomas and basal cell carcinomas, is less well known. Many studies in recent years have aimed at elucidating this association, with some yielding interesting findings. One such study, published by Karagas *et al.* in 2006, entitled "Human papillomavirus infection and incidence of squamous cell and basal cell carcinomas of the skin" found that patients with squamous cell carcinomas (n=252) had a higher incidence of HPV antibodies in serum compared to control patients (n=525). However, no such relationship was found between HPV antibodies in patients with basal cell carcinomas (n=461) (7). Another study, published by Chahoud *et al.* in 2016, entitled "Association between β-genus human papillomavirus and cutaneous squamous cell carcinoma in immunocompetent individuals-a meta-analysis", found that patients with increased levels of serological HPV antibodies were at an increased risk for developing cutaneous squamous cell carcinoma, supporting the conclusion that HPV may serve a role in HPV development and progression in healthy individuals (8).

The most recent study published by Nichols *et al.* has opened the door for scientists to discover if the HPV vaccine has applications in treating noncervical cancers. It is essential that more studies be done regarding the effectiveness and mechanism of the 9-valent HPV vaccine as a treatment for bSCCs. Information obtained from studies on this topic could be crucial in developing therapeutic vaccines and other immunotherapies for bSCCs and related cancers, which affect millions of patients throughout the world annually.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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