Category: Clinical Research

Title: Amplified Skin Cancer Risk in HPV-Positive Immunosuppressed Patients: A Multicenter Real-World Cohort Study

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Abstract

Background: Human papillomavirus (HPV) infection has well-established oncogenic potential in anogenital and oropharyngeal tissues, yet its role in cutaneous carcinogenesis remains incompletely defined. Immunosuppressed patients, including solid-organ transplant recipients and individuals receiving systemic corticosteroids or other immunosuppressive therapies, have an elevated risk of nonmelanoma skin cancers. However, the influence of concurrent HPV infection on this association is less well characterized. We evaluated whether HPV infection in the setting of systemic immunosuppression is associated with increased risk of cutaneous malignancy.

Methods: Using the TriNetX US Collaborative Network, we identified patients with documented HPV infection and concurrent immunosuppression defined by transplant status, long-term systemic corticosteroid use, or immunosuppressive medications. HPV-positive patients without immunosuppression served as controls. Propensity score matching balanced cohorts for age, sex, and race/ethnicity, yielding 245,027 patients per group. Outcomes included incident squamous cell carcinoma (SCC), basal cell carcinoma (BCC), melanoma, melanoma in situ, sebaceous carcinoma, Kaposi sarcoma, and other malignant neoplasms of the skin, excluding patients with prior diagnoses.

Results: Immunosuppressed HPV-positive patients demonstrated higher risks across multiple cutaneous malignancies compared with HPV-positive controls. SCC occurred in 1.0% versus 0.6% of patients (risk ratio [RR] 1.64, 95% CI 1.54–1.75; $p<0.001$), and BCC occurred in 1.3% versus 1.0% (RR 1.24, 95% CI 1.17–1.30; $p<0.001$). Melanoma incidence was modestly increased (RR 1.13, 95% CI 1.02–1.25; $p=0.023$). The largest relative increase was observed for sebaceous carcinoma of the eyelid (RR 3.65, 95% CI 2.13–6.24; $p<0.001$). Other malignant skin neoplasms were also more frequent among immunosuppressed patients.

Conclusion: HPV infection in the setting of systemic immunosuppression is associated with increased risk of several cutaneous malignancies. These findings suggest that impaired viral clearance and altered immune surveillance may contribute to cutaneous oncogenesis. Enhanced dermatologic surveillance and preventive strategies may benefit immunosuppressed patients with HPV infection.

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