Beta-HPVs Linked to Squamous Cell Skin Cancer

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BY JENNIE SMITH

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A new population-based study has demonstrated an association between a group of human papillomaviruses viruses and an increased incidence of squamous cell carcinomas, adding weight to the emerging body of evidence that one genus of HPV may play a role in nonmelanocytic skin cancers.

The findings showed that seropositivity to more than one of a host of 16 beta-HPV types increased the likelihood of being diagnosed with a squamous cell carcinoma. Moreover, the risk increased with the number of beta-HPV types to which a person tested positive. No particular type among the 16 examined was found to increase the risk more than another; the risk merely increased with the number of infections (BMJ 2010 Jul 9 [doi:10.1136/bmj.c2986]).

People with antibodies to two or three types of beta-HPVs were 1.4 times more likely to have been diagnosed with a squamous cell carcinoma than were healthy controls.

People positive for more than eight types of beta-HPV were 1.7 times more likely to have SCC.

However, no link was found between seropositivity to beta-HPVs and basal cell cancers.

For their research, the largest study to date to associate beta-HPV and squamous cell skin cancer in a general population, epidemiologist Margaret Karagas, Ph.D., of Dartmouth Medical School, Lebanon, N.H., and her colleagues identified and analyzed, from an existing cohort in and around the state, 663 previously diagnosed cases of squamous cell carcinoma and 898 cases of basal cell carcinoma, along with 805 randomly chosen healthy controls from the same region.

Study participants were aged between 25 and 75 years and nearly all were white. None of their carcinomas occurred in genital regions. All were interviewed and had venous blood drawn and analyzed for the presence of beta-HPV antibodies. A handful of cases—seven squamous cell and two basal cell, along with seven healthy controls—could not be included in the analysis because of problems with their samples.

Dr. Karagas and her colleagues performed subanalyses to identify confounding factors that would influence the risk of developing the cancers. "All risk estimates ultimately were adjusted for or stratified by age, sex, and sun sensitivity, and additionally for cigarette smoking for cases of squamous cell carcinoma," they wrote. "No other factors appreciably influenced the results."

Of particular interest to the investigators, though, was one subgroup of people taking glucocorticoids. Previous research had shown links between immunosuppressed organ transplant recipients, beta-HPV positivity, and another type of nonmelanocytic skin cancer (Transplantation 1996;61:715-21), so Dr. Karagas’ team identified cases and controls who had never had a transplant but had taken systemic glucocorticoids to treat other conditions to determine if glucocorticoid use, and not transplantation, might be the factor affecting the association.

They found that people who reported having taken glucocorticoids for at least a month did in fact have a higher incidence of squamous cell carcinoma with beta-HPV positivity. Notably, the investigators wrote, the odds ratio for squamous cell carcinoma with beta-HPV positivity was...
3.21 among participants with a history of prolonged glucocorticoid use, and 1.23 among those without such a history. The findings, they wrote, “suggest that the known association between the human papillomavirus and occurrence of skin cancer in the presence of immunosuppression extends to drugs more commonly used by the general population.”

Another potential risk factor Dr. Karagas and colleagues identified was ultraviolet exposure. “Though cases with a history of severe sunburn did not evidence higher cancer risk than that of controls with the same history, the findings that sun-sensitive people were at higher risk “provide some evidence of an interaction between exposure to ultraviolet light and human papillomavirus related risk of squamous cell carcinoma,” they wrote.

However, the investigators cautioned, the findings related to the sun-sensitive and glucocorticoid subgroups had limited statistical power. They also noted that because the vast majority of subjects were white, the findings could not necessarily be generalized further. Neither Dr. Karagas nor her colleagues declared any conflicts of interest.

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