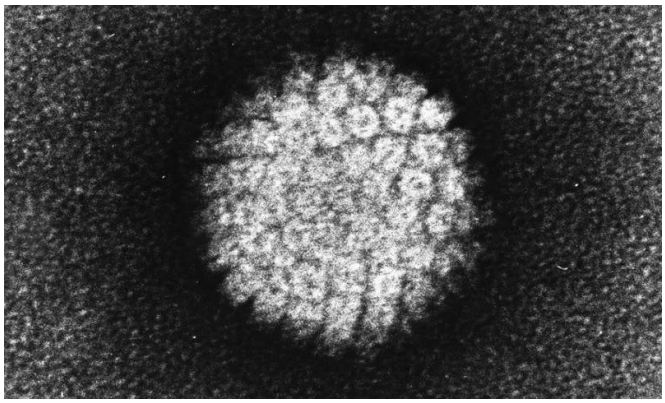
Particular HPV strain linked to improved prognosis for throat cancer

28 September 2016



Electron micrograph of a negatively stained human papilloma virus (HPV) which occurs in human warts. Credit: public domain

When it comes to cancer-causing viruses like human papillomavirus, or HPV, researchers are continuing to find that infection with one strain may be better than another.

In an analysis of survival data for patients with a particular type of head and neck cancer, researchers from the University of North Carolina Lineberger Comprehensive Cancer Center confirmed findings that a particular strain of HPV, a virus linked to a number of cancers, resulted in better overall survival for patients with oropharyngeal cancer than patients with other strains of the virus in their tumors.

They believe their findings, reported in the journal Oral Oncology, are particularly important as physicians move to lessen treatment intensity for patients with HPV-linked oropharyngeal cancer in clinical trials to try to spare them negative side effects of radiation or drugs. They also found that a test used widely to determine patients' HPV status may not be sensitive enough to select patients for de-intensification.

"What we demonstrate in this study is that the type of HPV can help us to better determine a patient's prognosis," said the study's senior author Jose P. Zevallos, MD, MPH, an associate member of UNC Lineberger and an associate professor in the UNC School of Medicine. "We think this is important because HPV positive patients do so well generally, and there's been a huge move nationally to take treatment down a couple notches to limit morbidity and side effects. The risk is that if you de-intensify too much, and you happen to have a high-risk tumor because you have a different type of HPV, then this could be harmful to patients who don't warrant it."

The UNC study was based on an analysis of survival data for 238 patients in North Carolina diagnosed between January 2002 and February 2006 with oropharyngeal cancer, a type of head and neck cancer in the throat at the back of the mouth, as part of the Carolina Head and Neck Cancer Study, or CHANCE. The Centers for Disease Control and Prevention estimates that more than 15,600 cases of HPV-associated oropharyngeal cancer are diagnosed in the United States each year.

Previous studies have shown that patients with HPV-linked oropharyngeal cancer have higher survival and lower recurrence rates compared to those with HPV-negative oropharyngeal cancer. As those patients tend to respond better to treatment, researchers are studying whether patients with HPV-linked oropharyngeal cancer can receive less intensive treatment with good outcomes. The researchers point out, however, that there has been limited research that tracks outcomes for oropharyngeal cancer based on the particular strain of HPV that patients have.

Zevallos and his colleagues confirmed earlier findings that patients with oropharyngeal cancer tumors infected with HPV16 had improved overall survival. They also determined that patients whose

cancer was infected with other HPV strains had similar survival rates as patients whose cancer did not have HPV at all.

They found that 71.4 percent of patients with HPV16-linked oropharyngeal cancer lived at least five years. Meanwhile, the five-year survival-rates for patients with other strains of the virus in their tumors, and for patients who were HPV-negative, were lower: 57 percent for patients with other types of HPV and 50 percent for HPV-negative patients.

Zevallos said the finding of a lower survival rate for patients positive for HPV strains other than HPV16 is important in that it indicates that those patients may not be good candidates for treatment de-intensification.

"The finding that non-HPV16 types are closer to the HPV-negative group in terms of survival differences suggests that those patients should definitely not be considered for anything other than standard aggressive therapy," he said.

The researchers noted that additional research needs to be done in a larger sample size to rule out the possibility that characteristics other than HPV status are driving survival differences, and to clarify whether the patients found to have other HPV strains were not false-positives.

The also cautioned that based on their findings, a commonly used clinical test that measures for the presence of the p16 protein may not be specific enough to identify HPV-linked oropharyngeal cancer patients who are good candidates for treatment de-intensification. To determine whether patients had HPV-positive tumors, they compared the results of the p16 test with results of a more specific genetic test.

They found that 4.3 percent of the patients were positive for p16, but negative for HPV according to the genetic test. Another approximately 11 percent of p16-positive cases had HPV strains other than HPV16, according to the genetic tests. Zevallos said this is an important finding because patients whose cancer was not infected with HPV16 had a lower 5-year survival rate, meaning they would not be good candidates for treatment de-escalation.

Yet the researchers report that many of the clinical trials that de-intensify treatment use p16 expression alone to determine if a patient's cancer is HPV-positive, and whether they should be considered for treatment de-intensification.

"Even though we rely almost exclusively around the country on p16 positivity as a surrogate for HPV16 presence, this sheds some light on the fact that maybe we should be considering HPV genotyping because of the survival differences we saw here," Zevallos said.

More information: Angela L. Mazul et al, Prognostic significance of non-HPV16 genotypes in oropharyngeal squamous cell carcinoma, *Oral Oncology* (2016). DOI: 10.1016/j.oraloncology.2016.08.019

Provided by University of North Carolina Health Care