Oropharyngeal cancer patients with human papillomavirus have more robust response to radiation therapy

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(Medical Xpress)—UC Davis cancer researchers have discovered significant differences in radiation-therapy response among patients with oropharyngeal cancer depending on whether they carry the human papillomavirus (HPV), a common sexually transmitted virus. The findings, published online today in *The Laryngoscope Journal*, could lead to more individualized radiation treatment regimens, which for many patients with HPV could be shorter and potentially less toxic.

HPV-related cancers of the oropharynx (the region of the throat between the soft palate and the epiglottis, including the tonsils, base of tongue and uvula) have steadily increased in recent years, according to the National Cancer Institute, especially among men. At the same time, the incidence of oropharyngeal cancers related to other causes, such as smoking or alcohol consumption, is declining. HPV is the most common sexually transmitted infection in the United States; it can spread through direct skin-to-skin contact during vaginal, anal and oral sex.

The UC Davis study, conducted by Allen Chen, associate professor in the UC Davis Department of Radiation Oncology, examined patterns of tumor reduction during radiation treatment in two otherwise similar groups of patients with oropharyngeal cancer: those who tested positive for HPV and those who tested negative for the virus. None of the HPV patients in the study was a smoker, a leading risk factor for the disease.

Chen used CT scans acquired during image-guided radiation therapy (IGRT) and endoscopy (a tube with a small camera) to capture 3D images of the patients' tumors and monitor their treatment progress. He found that within the first two weeks after starting radiation, the gross tumor volume decreased by 33 percent in HPV-positive patients, while the volume decreased by only 10 percent in HPV-negative patients.

Chen said the results demonstrate that HPV-positive patients have a more rapid and robust response to radiation treatments, confirming what clinicians have suspected for years.

"These HPV-related tumors literally melt before your eyes," he said. "It is very gratifying to tell patients early on during treatment that their tumors are responding so quickly. Most of them are pleasantly relieved to hear such news."

The rapid rate of tumor regression did not continue, however, after the second week of radiation treatment, and by the end of the seven-week regimen, the total tumor shrinkage in both groups of patients was nearly the same.

However, "the dramatic early response observed in the HPV-positive patients strongly implies that these tumors behave distinctly from a biological standpoint and could be approached as a separate disease process," Chen said.

For example, the findings suggest that treatment for HPV-positive cancer may not need to be as intensive for it to be effective, Chen said, adding that a shorter, abbreviated treatment regimen would potentially lessen the side effects from radiation, which include sore throat, dry mouth, taste loss and swallowing difficulties.

"It is likely that treatment in the future will be individualized based on

biomarkers present in the tumor, and HPV has the potential to do just that," said Chen.

Chen said there is increasing evidence that HPV-positive patients who receive radiation treatments live longer and have higher cure rates. According to the NCI, 88 percent of the HPV-positive patients are still alive two years after their treatments, compared with 66 percent of the HPV-negative patients.

"Given the impressive outcomes for patients with HPV-positive cancer using currently aggressive treatments, how to de-intensify therapy while maintaining cure rates is definitely a hot topic right now," said Chen.

Chen, in collaboration with colleagues, has recently launched a clinical trial of HPV-positive oropharyngeal cancer patients to evaluate outcomes when their radiation doses are reduced from seven weeks to either five or six, depending on their response to initial chemotherapy. This institutional trial, which is only available at UC Davis, just recently opened enrollment.

"Why subject a patient to seven weeks of radiation when five weeks of radiation could be just as effective?" Chen said. "Sparing select patients from this extra radiation could potentially prevent significant toxic side effects and improve quality of life, both in the short-term and long-terms."

The current clinical trial also involves collection of oropharyngeal patient blood and tumor samples during treatment, so that researchers can precisely correlate HPV in these specimens with a patient's rate of response to radiation therapy.

The dramatic increase in oropharyngeal cancers in recent years has been described as an "epidemic," Chen said, due in large part to the increasing

prevalence of HPV. In the United States, more than half of cancers currently diagnosed in the oropharynx are linked to HPV-16, according to the National Cancer Institute.

"Our trial was designed to help determine what the optimal treatment approach for these patients might be in the future," Chen said.

Why HPV-positive tumors respond differently to radiation treatment is under investigation at UC Davis, as well. The thought is that HPV labels cancer cells with a foreign antigen, which stimulates an immune response, Chen said.

"The HPV hijacks the host cancer cell leading to expression of a viral antigen on the surface, causing the patient's immune system to ramp up and fight the cancer," Chen said. "By identifying which molecular pathways are up-regulated or down-regulated during radiation therapy, it is our hope that insight may be gained into why HPV-positive oropharyngeal cancer is so radiation sensitive. This could have tremendous implications for developing strategies to fight not just oropharyngeal cancer, but all tumors in the future."

Provided by UC Davis