

HPV linked to better survival in tonsil, tongue cancer

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Researchers at the University of Michigan Comprehensive Cancer Center have found a series of markers that indicate which patients are more likely to survive cancers of the base of the tongue and tonsils.

Most notably, they found that cancers linked to HPV, or human papillomavirus, are the most responsive to current chemotherapy and radiation treatments, while tumors that express high levels of a certain growth factor receptor are the least responsive and most deadly.

The researchers call these and other markers a promising step in the direction of tailored, individualized treatment for a type of cancer that can have dramatic impact on essential abilities such as swallowing and speaking.

Results of the study appear in two papers published May 12 online in the *Journal of Clinical Oncology*. The papers will be published in the journal's July 1 print issue.

“The chemotherapy and radiation therapy we use to treat this type of cancer is very aggressive. If we can identify those patients most likely to respond, we could reduce the intensity of the therapy for those likely to have the best outcomes. At the same time, we hope to identify new treatments that specifically target those tumors that we know are not responding to current therapies,” says Thomas Carey, Ph.D., Professor and Distinguished Research Scientist at the U-M's Kresge Hearing Research Institute and co-director of the head and neck oncology

program at the U-M Comprehensive Cancer Center. Carey was the senior author on both papers.

Cancers of the tonsils and the base of the tongue have increased in recent years, in what Carey calls an “epidemic” of HPV-induced head and neck cancer. This has occurred at the same time that declines in smoking rates have led to a decrease in the incidence of other types of head and neck cancers. HPV is the virus that can cause cervical cancer and is the target of a new vaccine.

“The biggest challenge is how best to treat patients with tumors that stem from tobacco and alcohol use as opposed to tumors linked to HPV. We now know they’re two different cancers,” says study author Francis Worden, M.D., assistant professor of internal medicine at the U-M Medical School.

In this study, researchers treated 66 patients with advanced oropharyngeal cancer, which includes cancer of the tonsils and the base of the tongue. Study participants were given an initial course of chemotherapy to gauge the tumor’s response. Those whose tumor was reduced by more than half of its original size received a full course of chemotherapy and radiation given simultaneously. Patients whose tumors did not respond were referred for surgery.

Fifty-four of the 66 participants responded to the initial chemotherapy. Of that group, 62 percent are alive today without evidence of cancer, and 73 percent fully preserved their organs.

Participants whose cancer did not respond to the chemotherapy and radiation went on to receive surgery. The researchers found that even with surgery, only 4 of 11 patients survived.

“For most patients, the chemoradiation was very effective. But a subset

of patients still do not do well. Our next step was to look at the biomarkers to see if we could determine which patients were responding to treatment, based on the tumor biology,” says Carey, who is also associate chair and professor of otolaryngology and pharmacology at the U-M Medical School.

By looking biopsies taken before treatment, the researchers found 64 percent of the tumors were positive for high-risk strains of HPV. Almost all of the HPV-positive tumors responded to initial chemotherapy and 78 percent of those patients survived with their organs preserved. Of the HPV-negative study participants, only four of 15 survived. In addition, the researchers found that patients whose tumor expressed a marker called EGFR had worse outcomes.

“The combination of markers was an important indicator. Patients whose tumors expressed high levels of EGFR did poorly. But those who had high EGFR and were also HPV-positive had some protection. Patients with high EGFR and low HPV fared the worst. This is a step in the direction of affecting future treatment,” says Bhavna Kumar, a research laboratory specialist who was the lead author on both papers.

The researchers also found that tumors with low expression of a protein called p53, combined with high expression of another protein, BCLXL, also had poor outcomes. These markers provide additional targets for potential new therapies.

Source: University of Michigan Health System

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