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People with hepatitis C are two to five times more likely to develop certain head and neck cancers

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Long associated with liver cancer and non-Hodgkin's lymphoma, a study from The University of Texas MD Anderson Cancer Center reveals for the first time that the hepatitis C virus (HCV) is associated with certain head and neck cancers. The findings, published in the *Journal of the National Cancer Institute*, could have significant implications for both the screening of those with the virus and the treatment of those with head and neck cancers.

Hepatitis C, the most common blood-borne infection in the U.S., is a virus that affects up to 1.5 percent of the population. It's estimated that as many as 3.9 million are chronically infected with the virus, according to the researchers.

In the last few years, new antiviral drugs have made it possible to cure more than 90 percent of the HCV population, says Harrys A. Torres, M.D., associate professor, Infectious Disease, Infection Control and Employee Health. The antivirals are oral medications taken once or twice daily with almost no side effects, he explains.

In 2009, MD Anderson opened what remains the only clinic of its kind at a comprehensive cancer center to address the unmet medical needs of its patients with HCV.

"Obviously, a hepatitis C infection could impact how patients respond to

their cancer therapy. We also realized that many of our hepatitis patients were excluded from clinical trials. Now that many with hepatitis C can be cured, it is important that we first address and potentially cure the virus, so that they can have access to necessary cancer therapy."

When Torres started the clinic, he expected to see a number of patients with liver cancers and non-Hodgkin's lymphoma, as these have documented associations with HCV of 48-fold and two- to three-fold increased risk, respectively. Other recent studies have recognized HCV's increased association with additional cancers, says Torres, but there was no known association with a significant number of head and neck cancers.

"To our surprise, we saw a number of head and neck cancer patients who tested positive for the hepatitis C virus. With this observation we began to wonder if there was an undiscovered correlation between the two. Our findings tell us that the association between hepatitis C and oropharyngeal and nonoropharyngeal cancers is as high as its link to non-Hodgkin's lymphoma."

Oropharyngeal cancers occur in the oropharynx, or the middle part of the throat, including the back one-third of the tongue, the soft palate, tonsil, and side and back walls of the throat. Nonoropharyngeal cancers include those occurring in the oral cavity, nasal cavity and larynx.

For the retrospective, case-controlled study, the researchers identified 34,545 MD Anderson patients who were tested for HCV between 2004 and 2014. All patients were tested for HCV antibodies and viral RNA tests were used to confirm chronic infection, when available.

The researchers included 409 head and neck cancer patients as case subjects (164 with oropharyngeal and 245 with nonoropharyngeal). Also paramount to the research, said Torres, was to control for smoking, a

major risk factor for head and neck cancers. Therefore, they identified 694 control subjects, all with a diagnosis of smoking-related cancers (378 with lung, 168 with esophageal and 148 with bladder).

The study revealed that 14 percent of patients with oropharyngeal cancers tested positive for HCV antibodies, compared to just 6.5 percent in the control group. In those with nonoropharyngeal cancer, 20 percent tested positive for HCV antibodies. All findings were highly statistically significant.

Compared to the controls, the researchers found that the risk for HCV patients of developing specific head and neck cancers was increased 2.4 times for oral cavity cancers, 2.04 times for oropharynx cancers, and 4.96 times for larynx cancers.

Of note, 145 of all the oropharyngeal cancer patients were also tested for human papillomavirus (HPV), allowing researchers to compare possible associations between the two viruses. Patients with HCV-positive head and neck cancers were more likely to also test positive for HPV.

This finding, says Torres, is an area of great interest for future research study. Given the association found between the two viruses in this patient population, Torres and colleagues plan to look at other HPV-associated cancers and their possible link to HCV, under MD Anderson's Moon Shots Program.

Torres notes that it will be important to screen for HCV because treatment with antiviral drugs may possibly prevent cancer from ever developing, as reported for liver cancers and non-Hodgkin's lymphoma.

It may also impact treatment for patients who have already developed cancer. In fact, for patients with HCV and some indolent non-Hodgkin's lymphoma, Torres notes that the National Comprehensive Cancer

Network guidelines now recommend that the HCV be treated first, given that it is curable. In some cases, explains Torres, the lymphoma has disappeared upon treating the HCV with antiviral therapies.

With these findings, MD Anderson plans to screen and treat all head and cancer patients with HCV and follow their outcomes.

Educating both the general hepatology and infectious disease communities—those primarily treating patients with HCV—is critical so they understand HCV impacts not only the liver, but is a systemic infection.

"What we are trying to make all understand is that this is an infection that has consequences—and it's an infection we can cure," says Torres.

Provided by University of Texas M. D. Anderson Cancer Center

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