Researchers find genetic precursors of leukemia in patients treated for non-blood cancers

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Catherine Coombs, MD, is an associate member at UNC Lineberger and assistant professor in the UNC School of Medicine.

In a study of nearly 9,000 people treated for solid tumor cancers,

researchers found that radiation treatment and tobacco use were linked to higher rates of blood-based DNA mutations that could lead to higher risk for blood cancers like leukemia.

The study, published in the journal *Cell Stem Cell*, revealed new risk factors for "clonal hematopoiesis," a medical phenomenon in which genetic mutations are found in the blood cells of patients who do not have an existing blood cancer. Twenty-five percent of the patients in the study had clonal hematopoiesis. Of the subset of patients they actively followed, those with clonal hematopoiesis had a small – 1 percent – but increased, estimated incidence of developing blood cancer later on.

"The presence of clonal hematopoiesis can lead to an increased risk for subsequent blood cancers," said UNC Lineberger's Catherine Coombs, MD. "We wouldn't recommend forgoing treatment that is medically indicated because the risk of a secondary cancer is relatively low, but it is important to closely watch those patients who are high-risk."

Coombs was first author of the study at the Memorial Sloan Kettering Cancer Center in New York, where she completed a fellowship in oncology before coming to UNC Lineberger. The study analyzed genetic changes from 8,810 MSK cancer patients. The researchers found clonal hematopoiesis in 25 percent of patients, with the highest incidence in patients with thyroid cancer, and the lowest in patients with germ cell tumors. Mutations were more common in older people, with the odds of clonal hematopoiesis increasing 6 percent for each decade above age 30. Clonal hematopoiesis was also strongly associated with current or former tobacco use.

"A major risk factor for developing clonal hematopoiesis that can be modified or changed is tobacco use," Coombs said.

They also found a higher frequency of patients with clonal

hematopoiesis who had received radiation therapy. Forty-one percent of patients with clonal hematopoiesis received radiation, compared to 35 percent of patients who did not have clonal hematopoiesis, and had received radiation.

Risk for developing a secondary blood cancer was very small in the patient population overall. Only 19 out of the 5,394 patients the researchers actively followed developed a new blood cancer within 18 months. However, for patients who did get a blood cancer, the risk was higher for patients who had clonal hematopoiesis. One percent of patients with clonal hematopoiesis were estimated to develop a secondary cancer, which was three times higher than the estimated 0.3 percent for patients who developed blood cancer and did not have clonal hematopoiesis.

"This has been borne out by other groups: if you have these clonal hematopoiesis mutations, you have a greater risk for developing hematologic cancer than do patients who don't have them," she said.

Coombs said more research is needed to determine the cause of these increases.

More information: Catherine C. Coombs et al. Therapy-Related Clonal Hematopoiesis in Patients with Non-hematologic Cancers Is Common and Associated with Adverse Clinical Outcomes, *Cell Stem Cell* (2017). DOI: 10.1016/j.stem.2017.07.010

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