Study finds dysfunctional white blood cells linked to heightened melanoma risk

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About 8 to 10 million Americans over age 40 have an overabundance of cloned white blood cells, or lymphocytes, that hamper their immune systems. Although many who have this condition—called monoclonal B-

cell lymphocytosis (MBL)—do not experience any symptoms, a new study shows they may have an elevated risk for several health complications, including melanoma, a form of skin cancer.

The findings, by Mayo Clinic researchers, are published in a new paper in the *Journal of Clinical Oncology*.

People with MBL fall along a spectrum that spans from a low amount to a high amount of these dysfunctional lymphocytes. Previous research has shown that MBL is a precursor to a type of blood and bone marrow cancer known as chronic lymphocytic leukemia (CLL). People with CLL also have a heightened risk of melanoma.

"Our study is the first to show that people with this pre-cancerous stage of MBL have a 92% elevated risk of developing melanoma. The risk of melanoma is similar to what we see among people with chronic lymphocytic leukemia," says Susan Slager, Ph.D., researcher with the Mayo Clinic Comprehensive Cancer Center and senior author of the study.

The findings suggest that having MBL, even at low levels, can serve as a biological signal, or biomarker, for early detection of melanoma, which is increasing worldwide.

Dr. Slager and her research team have been studying the largest available cohort of individuals—more than 7,000 people screened for MBL through the Mayo Clinic Biobank. The researchers have now followed these individuals for about four years and are finding a collection of potentially related diagnoses among those who screened positive for MBL.

In addition to the increased risk of melanoma, the researchers found that people with MBL were also at higher risk of cancers originating in the

lymphatic system and hospitalizations due to serious infections including from COVID-19.

"Previously, scientists would equate MBL as just a part of the aging process. What we're seeing, though, is there are clinical consequences to having MBL—contracting serious infections and melanoma are some of them," Dr. Slager says.

Technological advances provide a closer look

Advances in flow cytometry, a high-resolution technology that enables researchers to look at cells in the blood and identify their varied physical characteristics, has helped propel this research. Clinicians and researchers can now identify people with MBL, the precursor to CLL, more easily.

People with CLL have a very high number of these identical circulating lymphocytes: more than 5,000 lymphocytes per microliter. (A microliter is about 1/50th of a drop of blood.) That's compared to a person with MBL, who typically has one to five of these circulating lymphocytes per microliter of blood. Through more sensitive flow cytometry, scientists can identify people earlier when their levels are still low.

"The risk of melanoma seems to be the same no matter how many of these cloned lymphocytes are in the blood, suggesting that just having a clonal population of these lymphocytes—meaning, having MBL—increases your risk of getting melanoma," she says.

Patients with CLL are encouraged to get annual skin cancer screenings by a dermatologist and to protect their skin from sun exposure to prevent melanoma.

"Our findings suggest that people with the precursor MBL stage should

also be more diligent about following the established guidelines for skin cancer prevention including, for example, use of sunscreen and protective clothing," Dr. Slager says.

Next steps

One of the questions Dr. Slager's team plans to explore next is whether there is a genetic overlap between MBL, CLL and melanoma. One hypothesis is that inheriting a genetic variant that increases the risk of MBL and CLL may also increase the risk of melanoma.

Another area the researchers are investigating is whether MBL impacts the clinical outcome among people with melanoma, including if having both MBL and melanoma reduces one's overall survival or affects a person's response to therapy.

More information: Bryan A. Vallejo et al, Risk of Incident Melanoma Among Individuals With Low-Count Monoclonal B-Cell Lymphocytosis, *Journal of Clinical Oncology* (2024). DOI: 10.1200/JCO.24.00332

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