Medical Xpress

Stress linked to more advanced disease in some leukemia patients

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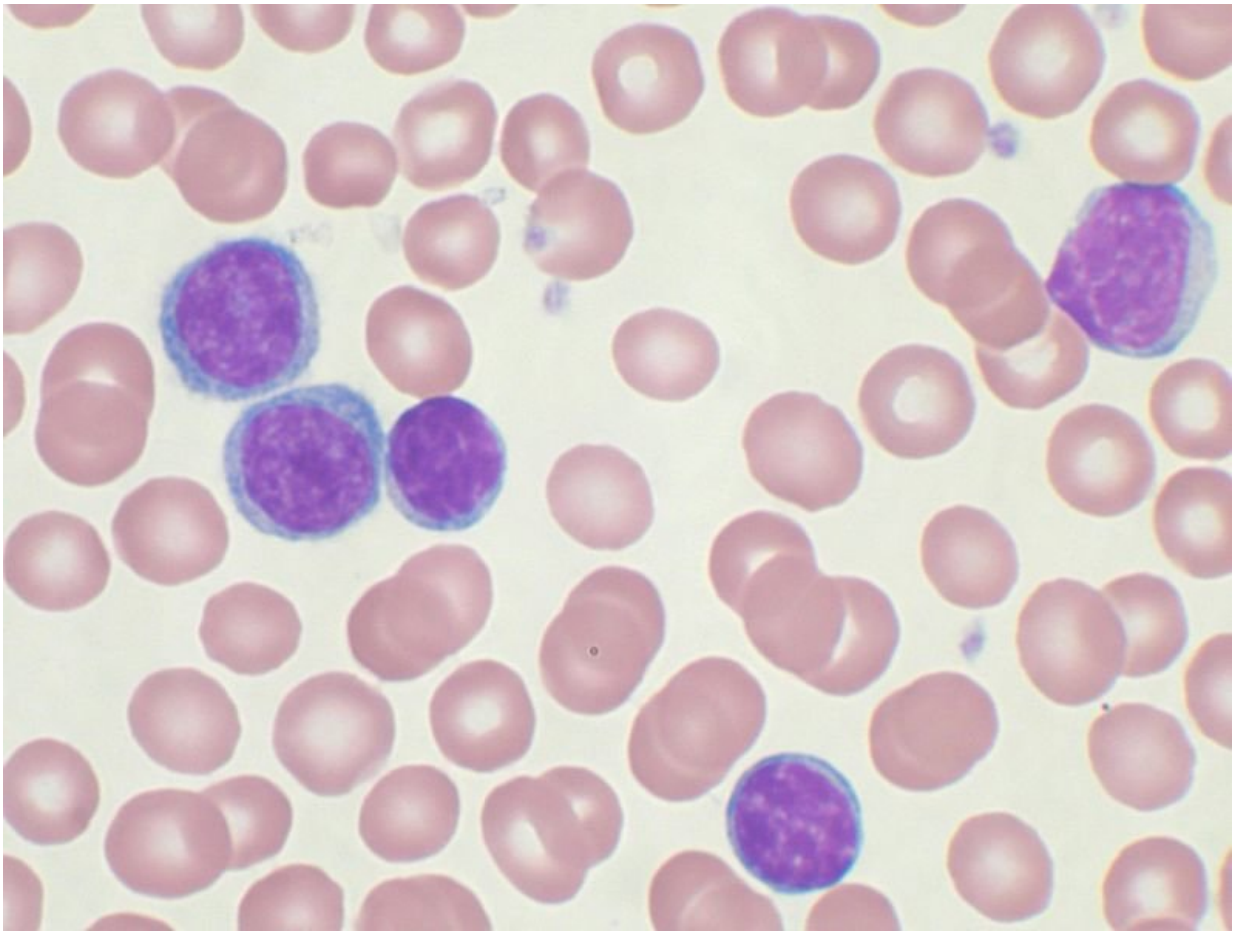

Credit: The Ohio State University

Patients with chronic lymphocytic leukemia (CLL) who feel more stress

also have more cancer cells in their blood and elevated levels of three other markers of more advanced disease.

A new study of 96 patients is the first to link stress with biological disease markers in patients with CLL.

"All four variables we measured are related to prognosis in CLL patients, so they have a lot of relevance," said Barbara L. Andersen, lead author of the study and professor of psychology at The Ohio State University.

"It's more evidence of the importance of managing stress in cancer patients."

The study appeared Aug. 1 in the journal *Cancer*.

CLL is the most common leukemia in adults, and accounts for about one-third of adult leukemia in the United States.

The study involved patients who were entering a trial at Ohio State's Arthur G. James Cancer Hospital for ibrutinib, now approved by the U.S. Food and Drug Administration. At the time of the study, the drug was in early trials to treat the disease. Data collection was done before patients received the first dose.

All patients completed a survey that measured their cancer-related stress. They were asked questions like how often they had intrusive thoughts about their cancer, how often they tried to avoid thinking about it and how often they felt jumpy and easily startled.

The researchers took blood samples and calculated absolute lymphocyte counts (ALC), which is a measure of healthy and malignant cells circulating in the blood. This measure is often elevated in patients with CLL and is used as a marker of disease severity. They also measured

levels of eight different cytokines, which are proteins involved in the body's immune response. All of these cytokines can promote unhealthy levels of inflammation in patients with cancer.

Results showed that more stress in the patients was associated with a higher number of circulating cancerous cells and higher levels of three cytokines: tumor necrosis factor alpha, interleukin 16 and chemokine ligand 3 (CCL 3).

CCL3 is a particular kind of cytokine called a chemokine. It helps facilitate the development of CLL cells in places like the spleen and lymph nodes, where leukemia cells are produced.

"Chemokines have not been used in studies like this before and it is a novel way of checking for the link between stress and disease," Andersen said.

Stress was linked to disease severity even after the researchers took into account several other important factors that also play a role in disease progression, including gender, the number of prior treatments and the presence of a genetic marker (del17p) that is associated with harder-to-treat CLL.

"The fact that stress shows an effect on CLL even after we controlled for other factors suggests it may be relevant to the course of CLL," Andersen said.

Why did the other five cytokines the researchers studied not show an effect in this study?

Andersen noted that this was the first study of its kind done with leukemia patients. Many of the other cytokines have been found to have effects in solid tumors and might not work the same way in blood

cancers.

The researchers are continuing to follow these patients and will examine the relationship between stress and these same responses throughout treatment, Andersen said.

More information: Barbara L. Andersen et al. Cells, cytokines, chemokines, and cancer stress: A biobehavioral study of patients with chronic lymphocytic leukemia, *Cancer* (2018). DOI: 10.1002/cncr.31538

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