Aggressive therapy best for certain acute myeloid leukemia patients

Medical Studies/Trials
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A new study suggests that acute leukemia patients whose cancer cells show a genetic change that usually predicts a swift return of the disease following remission may remain disease-free longer when given aggressive therapy.

The findings apply to people with acute myeloid leukemia (AML) whose cancer cells have normal-looking chromosomes and a gene mutation called MLL-PTD.

Typically, these AML patients responded poorly following treatment with older standard therapies, often relapsing within a year. Of AML patients with normal chromosomes who lack the mutation, on the other hand, four in 10 are cured.

The new study suggests that treating patients who have the mutation with an aggressive therapy such as an autologous stem cell transplant while they are in remission might significantly extend their disease-free survival.

An autologous transplant uses stem cells taken from the patient's own blood.

The research was led by investigators at the Ohio State University Comprehensive Cancer Center. It is part of a larger study sponsored by the Cancer and Leukemia Group B (CALGB), a clinical cooperative group composed of oncologists from academic medical centers and community hospitals across the nation.

The findings were published in a recent issue of the journal Blood.

"Our data is the first to show that AML patients with normal-looking chromosomes and this mutation do as well when treated aggressively as patients who don't have the mutation," says principal investigator Clara D. Bloomfield, professor of internal medicine and an internationally known AML specialist.

About 13,400 new cases of AML are expected this year, and

about half will have cancer cells with chromosomes that show distinctive damage. The nature of that damage helps doctors determine a patient's therapy and estimate the patient's prognosis.

The remaining AML cases have cancer cells with normal-looking chromosomes. These cells lack the microscopic chromosome damage that guide therapy.

In 1994, however, a team of researchers that included Bloomfield discovered the MLL-PTD mutation in these patients. It was the first clinically useful marker to be identified in cases of AML with normal-looking chromosomes, and it was found to predict a short remission and poor response to therapy. About 8 percent of AML patients with normal-looking chromosomes have the mutation.

"Studies done eight to 10 years ago showed that nearly 100 percent of these patients relapsed and died within two years," says first author Susan P. Whitman, a research scientist at Ohio State's Comprehensive Cancer Center.

This retrospective study set out to learn whether aggressive therapy provided through two CALGB clinical trials benefits patients with the mutation. It evaluated 238 people aged 18 to 59 with AML and normal-looking chromosomes. Of these, 24 (10 percent) had the MLL-PTD mutation.

All patients received an initial aggressive chemotherapy regimen (i.e., induction therapy) to induce remission. Those who achieved remission then received further aggressive therapy (i.e., consolidation therapy), usually an autologous stem cell transplant, with a few receiving intensive chemotherapy.

Of the 24 patients with the mutation, 22 had a complete remission. Of those, 13 relapsed within 1.4 years, but nine (41 percent) remained in remission when the study ended, with disease-free periods ranging from two to almost eight years.

"We believe that the use of aggressive consolidation therapy may have contributed to the reduced number of early relapses in these patients," Bloomfield says.

"We still must do larger studies to confirm these findings, to better understand this disease and to develop curative targeted therapies."

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