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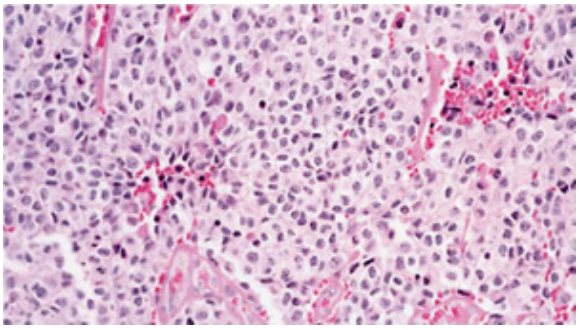
Featured Article

Genetic Abnormality Predicts Treatment Benefit for Patients with Rare Brain Tumor



Cells from a slice of tissue of an oligodendgroglioma tumor

The addition of chemotherapy to radiation therapy doubled the median survival time for certain patients with an aggressive form of oligodendroglioma, a rare brain tumor. Patients in the study had anaplastic oligodendrogliomas, but only those whose tumors contained a genetic abnormality known as the 1p19q co-deletion experienced a benefit from adding chemotherapy to radiation.

The finding, from a phase III trial in which patients were followed for a median of 11 years, will lead to changes in an ongoing NCI-sponsored clinical trial as well as in the standard of care for patients who are not enrolled in a clinical trial. NCI and the Radiation Therapy Oncology Group (RTOG) announced the finding January 19 in coordinated press releases (here and here).

Among patients whose tumors carried the abnormality, those treated with chemotherapy and radiation survived a median of 14.7 years, compared with a median of 7.3 years for those who received radiation alone.

The investigators took the unusual step of announcing the findings publicly before presenting them at a scientific meeting because of their importance for the treatment of other brain tumor patients.

"We wanted to share this information to ensure that patients have access to the most effective therapy," said Dr. Walter Curran of Emory University, a senior author of the study and RTOG group chairman. RTOG conducted the trial, known as RTOG 9402, in collaboration with four other NCI-sponsored cooperative groups.

In the trial, which began in 1994, 291 patients with oligodendrogliomas were randomly assigned to receive either standard therapy with radiation alone or radiation plus a multidrug chemotherapy regimen consisting of the drugs procarbazine, lomustine, and vincristine (PCV).

Results at a minimum follow-up time of 3 years, published in 2006, showed no overall survival benefit

for the patients who received chemotherapy. Regardless of treatment assignment, however, patients whose tumors carried the 1p19q co-deletion survived significantly longer than those whose tumors did not have the co-deletion (more than 7 years versus 2.8 years).

The new analysis, based on much longer follow-up of over 11 years, provides "strong evidence that the chromosomal structure of 1p and 19q co-deletion can be used as a marker to determine which patients will benefit from combined chemotherapy and radiation therapy," said principal investigator Dr. Gregory Cairncross of the University of Calgary in Canada.

Oligodendrogliomas, tumors that form in the brain's nerve tissue, make up about 9 percent of all primary tumors of the brain and central nervous system. They occur primarily in adults; the average age at diagnosis is 35. Roughly half of patients have tumors that contain the 1p19q co-deletion, in which parts of chromosomes 1 and 19 are simultaneously deleted.

The new findings mean that "initial management with radiation and chemotherapy should be considered the standard of care for patients with the co-deletion because of the survival benefit," said Dr. Curran.

For patients whose tumors contained only one chromosomal deletion (either 1p or 19q) or no deletion, survival was similar whether they received radiation alone or radiation plus chemotherapy (2.6 years versus 2.7 years).

The announcement of the findings resulted in immediate suspension of enrollment in an ongoing NCI-sponsored clinical trial in which patients with an aggressive brain tumor, anaplastic glioma, with the 1p19q co-deletion were being randomly assigned to treatment with radiation alone or radiation plus chemotherapy with the drug temozolomide. This international trial, dubbed CODEL, had been enrolling patients across North America and in Europe.

"Because our trial showed that treatment with radiation alone is inferior to chemotherapy plus radiation in patients with the co-deletion, it became necessary to immediately suspend accrual to CODEL and consider how the trial should be altered and how patients randomized to radiation therapy alone should be managed," Dr. Cairncross wrote in an e-mail.

"We cannot continue randomly assigning patients whose tumors have the 1p19q co-deletion to the radiation-only treatment arm now that we know chemotherapy plus radiation is superior," said Dr. Malcolm Smith of NCI's Cancer Therapy Evaluation Program, which oversees trials conducted by NCI-supported cooperative groups. "Patients not enrolled in clinical trials should also benefit from this new information."

Dr. Cairncross and his co-authors have submitted an abstract of the trial results for presentation at the American Society of Clinical Oncology annual scientific meeting in Chicago in June.

—Eleanor Mayfield

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