Preop Depression Linked to Shorter Brain Tumor Survival

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — Patients suffering from depression at the time they underwent surgery for malignant brain tumors had significantly worse survival compared with nondepressed patients in a retrospective analysis of 1,052 patients.

Although no causative association can be inferred because of the study’s retrospective design, recognizing and treating preoperative depression could maximize survival in patients with malignant brain tumors, Dr. Alfredo Quiñones-Hinojosa said at the annual meeting of the American Association of Neurological Surgeons.

Currently, patient age, tumor grade, and functional status are known preoperative prognostic indicators of survival. Identification of any reverse causation would be important, as malignant astrocytoma, also known as glioma or glioblastoma multiforme, typically results in death in about 1 year, even with the latest, most effective therapies.

Researchers at Johns Hopkins University in Baltimore, led by Dr. Matthew J. McGirt, analyzed the outcomes of 1,052 patients with malignant astrocytoma who underwent surgery from 1995 to 2006. Of these patients, 605 underwent primary resection, 410 underwent secondary resection, and 37 had a biopsy only. Excluding the biopsies, 213 tumors were World Health Organization grade III and 862 tumors were grade IV.

A total of 204 patients received subtotal resection, 274 received adjuvant therapy, and 136 required subsequent resection.

Only 49 patients (5%) who were found to be taking antidepressant medication for clinical depression at the time they underwent surgery met the study’s definition of having depression. All demographic and clinical characteristics were similar between the two groups, said Dr. Quiñones-Hinojosa.

Their mean age was 51 years and median preoperative Karnofsky Performance Scale (KPS) score was 80. Among survivors, the median postoperative follow-up was 12 months (range 3-18 months).

In a Kaplan Meier analysis, patients with depression had less than a 40% increase in the relative risk of mortality compared with nondepressed patients (relative risk 1.41), regardless of KPS, WHO tumor grade, patient age, or clinical presentation. This association was independent of extent of resection and postoperative treatment with either adjuvant temozolomide chemotherapy or Gliadel wafer use, Dr. Quiñones-Hinojosa said.

Median survival was 7 months among patients with depression, vs. 11 months in those without depression.

At 2 years post surgery, 5% of patients with depression were alive, compared with 23% of nondepressed patients. The difference was significant, he said.

Dr. Quiñones-Hinojosa acknowledged that the investigators could not be certain that the patients’ depression was not a response to the recent diagnosis of a terminal disease. In addition, many patients with clinical depression may have been undiagnosed and unmedicated, lowering the sensitivity of the classification scheme.

Discussant Stephen B. Tatter, a neurosurgery professor at Wake Forest University, Winston-Salem, N.C., said treating depression in this patient population is important as it might influence a variety of patient decisions, particularly when to stop treatment. “We don’t want just to prolong life but to provide quality that is acceptable to patients,” Dr. Tatter said.

Modafinil Reduced Severe Fatigue in Cancer Patients

BY KERRI WACHTER
Senior Writer

CHICAGO — The wakefulness-promoting drug modafinil (marketed asProvigil) reduced self-reported severe fatigue in a small breast cancer cohort, according to a recent study of more than 600 cancer patients who were undergoing chemotherapy.

Gary R. Morrow, Ph.D., of the University of Rochester (N.Y.) and his colleagues randomized 631 patients undergoing four cycles of chemotherapy to receive either 200 mg modafinil daily or placebo. Among those with severe fatigue at baseline, patients on modafinil had significantly greater reductions in fatigue compared with those on placebo.

Dr. Morrow presented his study’s findings at the annual meeting of the American Society of Clinical Oncology.

Study participants were asked to rate their level of fatigue at baseline (during the second cycle of chemotherapy) and during the final cycle.

They rated fatigue on a 10-point scale: mild (1-4), moderate (5-6), and severe (7-10).

A total of 67 patients reported mild fatigue at baseline; 106 and 438 reported moderate and severe fatigue, respectively.

Among patients with mild and moderate fatigue, modafinil also reduced fatigue, compared with placebo, but the differences were not significant.

This was not surprising, Dr. Morrow commented during a press briefing.

With side effects, quite often the patients feel, ‘the effect is some- what dependent on where you begin,’ he said.

Modafinil—a nonamphetamine stimulant—is currently indicated for the treatment of excessive sleepiness resulting from obstructive sleep apnea, shift-work sleep disorder, and narcolepsy. Last year, researchers also at the University of Rochester reported success with modafinil in treating “chemo-brain,” a reduction in cognitive function also thought to be associated with chemotherapy.

There may be some overlap between chemo-brain and fatigue, Dr. Morrow said in an interview. Problems with executive function are commonly described in chemo-brain.

Cancer-related fatigue appears to particularly affect tasks associated with executive function.

Cancer patients complain of not being able to “get around” to doing things they know they should do.

The pharmaceutical company Cephalon Inc. provided modafinil and placebo for the trial.

Dr. Morrow reported that he has no relevant financial relationships to disclose.

No Evidence of ‘Chemobrain’ in Small Breast Cancer Cohort

BY DENISE NAPOLI
Assistant Editor

CHICAGO — Chemotherapy-related cognitive impairment was infrequent in a small study of 30 patients who underwent adjuvant chemotherapy for non-metastatic breast cancer.

“People could be making decisions about whether or not to have chemotherapy based on stories they’ve heard about ‘chemo-fog’ or ‘chemobrain,’ ” according to Dr. David G. Darby. “We hope this information will help people make informed decisions.”

Dr. Darby and his colleagues looked at a total of 30 women who had already undergone either lumpectomy or mastectomy and were scheduled to undergo either the commonly used AC regimen known as AC (n = 15) or CEF or CMF regimens (n = 15).

The AC regimen involves cyclophosphamide administered orally in doses of 75 mg/m² on days 1-14; epirubicin 60 mg/m² by IV on days 1 and 8; and 5-fluorouracil 500 mg/m² by IV on days 1 and 8, repeated every 28 days for six cycles.

The CEF regimen involves cyclophosphamide 100 mg/m² given orally on days 1-14; methotrexate in doses of 40 mg/m² on days 1 and 8; and 5-fluorouracil 600 mg/m² IV on days 1 and 8, repeated every 28 days for six cycles.

Women took several tests designed to measure cognition as well as mood a few days before initiating chemotherapy (but after the diagnosis had been given and treatment course was decided); again at the start of each new treatment cycle; and for the last time 28 days after the treatment cycle had begun in each group. Patients were assessed on the National Institute of Mental Health’s Center for Epidemiologic Studies Depression Scale (CES-D) depression, the state trait anxiety inventory (STAI) scale, and a test of Dr. Darby’s own design, which measures detection speed, identification speed, working memory, and learning ability in a 10- to 12-minute battery.

Dr. Darby is the chief medical officer of a company he formed, called CogState, which produces and scores these tests. It is based in Australia and partly funded this study.

The first finding of interest was that prior to the first cycle of chemo there was impairment in learning of moderate amplitude, and that was also associated with a mild reduction on mood scales (CES-D, STAI) and then improve, and others would have impairment on two or more occasions,” he said. Persistent improvement that oc- curred on two consecutive oc- casions, was seen in only three patients, or 10% of the total, Dr. Darby reported at the annual meeting of the American Acade- my of Neurology.

Impairment in concentration was not severe, “equivalent to the sort of jet-lag that I’m feeling now, having traveled from Australia.”

He also likened it to the sort of impairment one would feel after being awake for about 17 hours.

Dr. Darby found no significant differences in the risk for cogni- tive impairment based on the women’s age, menopausal status (pre-, peri-, or post-), or time from surgery.

“When women are con- fronting breast cancer, coming to terms with the many different aspects of it, and trying to take advice and understand what’s happening to them, the issues of quality of life are important. They should realize that these sorts of changes seem to be very mild. They are present in a mi- nority of women, and they can be measured as well, if need be. In general, discussion with the patients about the mildness of these sorts of changes is probably the most appropriate [course for the treating physician],” said Dr. Darby.

Byline and Copyright: Denise Napoli