Long-term survival of patients treated with BCNU for brain tumors

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The authors present three patients who, after excision and irradiation of their brain tumors, were treated with BCNU for recurrence. All three patients responded well and now are without evidence of tumor, 37, 30, and 36 months after BCNU was stopped. Although these patients represent only a small fraction of those treated with BCNU, they indicate the potential role of chemotherapy in the management of glial tumors.

KEY WORDS • brain tumor • chemotherapy • survival • 1,3 bis (2-chloroethyl)-1-nitrosourea • BCNU

UNTIL recently malignant gliomas have been treated by surgical removal, as complete as possible, usually followed by adjuvant radiation therapy. Chemotherapeutic agents have been added to this regimen on a systematic trial basis in some centers. 1,3 bis (2-chloroethyl)-1-nitrosourea (BCNU) was found to be particularly effective against gliomas in preliminary studies,8,9 and has been the subject of a randomized study of its effects against malignant gliomas with and without radiation therapy.7

We are reporting three patients treated with BCNU for their recurrent gliomas. These cases are remarkable for the great length and excellent quality of survival.

Case Reports

Case 1

On October 7, 1968, a 14-year-old boy underwent posterior fossa exploration with removal of a fourth ventricular ependymoma (Fig. 1) and insertion of a Torkildsen shunt. He then received radiation therapy of 5000 rads to the posterior fossa. Improvement was transient, and in the spring and summer of 1969, he developed increasing ataxia, left facial weakness, left ptosis, and diplopia on downward gaze. Serial brain scans showed an increasing area of abnormal uptake in the posterior fossa (Fig. 2) and an air study showed displacement of the fourth ventricle to the right. Spinal fluid cytology showed
Flo. 1. Case 1. Photomicrograph showing grouping of cells and perivascular arrangement that led to diagnosis of ependymoma. H & E, × 200.

Case 1

This 49-year-old man developed seizures characterized by speech arrest, which led to the intratumoral removal of a left parietal anaplastic astrocytoma on September 10, 1969 (Fig. 3). Following surgery he received approximately 5000 rads whole brain radiation therapy. In December, 1969, he experienced a mild right hemiparesis and difficulty in reading. Angiographic studies in-

many neoplastic cells consistent with ependymoma. Therapy with BCNU was started in September, 1969. Initially he received 90 mg/m² of body surface daily for 3 days at 6- to 8-week intervals. The dose was reduced when he developed cumulative bone marrow toxicity. In all, he received 13 3-day courses of BCNU, the last in May, 1971. During the administration of chemotherapy his ataxia and diplopia cleared, leaving a minimal left facial weakness, mild right hemiparesis, and mild truncal ataxia. He also has atrophy of the sternal portion of the right pectoralis major muscle. Follow-up brain scans showed progressive lessening of the abnormalities (Fig. 2). He is currently employed as a manual laborer and is taking lessons in karate.

Case 2

This 49-year-old man developed seizures characterized by speech arrest, which led to the intratumoral removal of a left parietal anaplastic astrocytoma on September 10, 1969 (Fig. 3). Following surgery he received approximately 5000 rads whole brain radiation therapy. In December, 1969, he experienced a mild right hemiparesis and difficulty in reading. Angiographic studies in-

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Survival with BCNU treatment for brain tumors

dicated a large amount of residual tumor (Fig. 4 upper), and BCNU therapy was initiated at a dose level of 100 mg/m² daily for 3 days every 6 to 8 weeks, with dose reductions when bone marrow toxicity occurred. He received 10 courses of BCNU, the last in April, 1971. Motor and speech function improved steadily, and were normal 13 months after cessation of therapy. Follow-up angiograms (Fig. 4 lower), and scans (Fig. 5), indicate that the abnormality has markedly decreased.

Case 3

This 41-year-old man had a craniotomy for a left temporal lobe astrocytoma in 1962. Following this he received 5000 rads midplane whole brain radiation therapy. He was well and fully employed until the spring of 1969, when he developed dizziness, fatigue, and personality change caused by recurrence of the tumor. The tumor was resected (Fig. 6), but the patient's improvement was transient. Examination in November, 1969,
revealed a right hemiparesis. The site of the subtotal decompression was bulging, and arteriograms (Fig. 7 left pair) and brain scans (Fig. 8) indicated a large mass in the left temporal area.

In January, 1970, the patient was started on BCNU 80 mg/m² daily for 3 days every 6 to 8 weeks, with adjustments for bone marrow toxicity. He received 13 courses, the last in November, 1971. The decompression site rapidly became flat, and by July, 1970, the hemiparesis was minimal and has since been stable. The abnormality visible on arteriogram and brain scan progressively decreased (Figs. 7 and 8). The patient has a mild but persistent reduction of the white blood count.

Discussion

These patients vary in histological diagnosis and site of tumor. Two showed clinical and radiological progression of their mass lesions immediately prior to the initiation of therapy with BCNU. The third patient had evidence of a persistent large mass. The expected survival for each patient was very
short at the time therapy was started.2,4,6
All three patients showed clinical improvement and radiological evidence of lessening of their abnormalities under chemotherapy. Survival, without evidence of recurrence, is 56, 53, and 52 months from the initiation of chemotherapy; 36, 37, and 30 months from the end of chemotherapy (as of May, 1974). Quality of survival is excellent.

Unfortunately, these three patients represent less than 5% of those entered in the BCNU Phase II Study, so their results are more an indication of possibilities for the future than of immediate therapeutic gains. The mechanisms by which such survivals come about are elucidated by a surgical analogy. Jelsma and Bucy2,4 reported a large series of patients with glioblastoma mul-

**Fig. 7. Case 3. Angiograms taken January 20, 1970, (upper) and March 26, 1970 (lower).**
tiforme, with a few very long and excellent survivals. Each of these patients had had radical removal of the tumor, large areas of more benign-appearing tumor accompanying the glioblastoma, and postoperative radiation therapy. In our patients reported above, a similar radical removal of tumor was accomplished by chemical means.\(^1\)

The exquisite sensitivity of these patients' tumors to BCNU is reported as a matter of record. The achievement of excellent results in a few patients offers promise for the future of chemotherapy in the treatment of brain tumors; there is a need to identify other effective agents while efforts to select specific drugs for specific tumors continue.

**References**


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