Combination Chemotherapy with Carmustine and Cisplatin Followed by Procarbazine, Lomustine, and Vincristine for Adult High-Grade Astrocytoma

Chi-Ting Liau, MD; Kuo-Chen Wei[1], MD; Chen-Kan Tseng[2], MD; Shih-Ming Jung[3], MD

Background: We have reported that carmustine (BCNU) and cisplatin administered before, during, and after radiotherapy did not improve the survival of patients with high-grade astrocytomas and were associated with more serious toxicities than radiotherapy plus BCNU. In an attempt to improve survival, we studied a combination regimen procarbazine, lomustine, and vincristine (PCV) after radiotherapy in addition to BCNU and cisplatin during radiotherapy.

Methods: From 1994 through 1998, 42 patients were enrolled in the study. Of these, 20 had glioblastoma multiforme and 22 had anaplastic astrocytoma. The patients had a median age of 48.5 years. All patients had subtotal or total resection, or biopsy as the initial procedure. Then, all patients were treated with BCNU and cisplatin concurrently during radiotherapy followed by PCV after radiotherapy.

Results: The median time to follow up for survivors was 13.8 months (range, 1.7-108.2 months). The median time to tumor progression was 7.2 months (range, 0-88.7 months) and median survival time was 13.3 months (range, 1.7-88.7 months). The only factor that had a conventionally significant effect on the overall survival was resectability. Patients who had received subtotal/total resection had a longer median survival compared with patients who had received biopsy only (18.0 vs. 9.5 months). This combined modality treatment program was associated with reversible grade 3 to 4 hematological toxicity in 10 patients, with grade 3 ototoxicity in one patient and grade 2 neurotoxicity in one patient.

Conclusion: A combination of BCNU and cisplatin with cranial irradiation followed by PCV was moderately toxic and appeared to offer no obvious survival advantages compared with radiotherapy plus BCNU and cisplatin alone.

(Chang Gung Med J 2005;28:16-23)

Key words: chemotherapy, radiotherapy, glioblastoma multiforme, anaplastic astrocytoma.

Primary central nervous system malignancies represent less than 2% of all malignant diseases and of these more than 40% are malignant gliomas. Conventional treatment of patients with malignant

From the Division of Hematology Oncology, Department of Internal Medicine; [1]Division of Neurosurgery, Department of Surgery; [2]Department of Radiation Oncology; [3]Department of Pathology, Chang Gung Memorial Hospital, Taipei.

Received: May 12, 2004; Accepted: Nov. 18, 2004

Address for reprints: Dr. Chi-Ting Liau, Division of Hematology-Oncology, Department of Internal Medicine, Chang Gung Memorial Hospital. 5, Fushing Rd., Gueishen Shiang, Taoyuan, Taiwan 333 R.O.C. Tel.: 886-3-3281200 ext. 2524; Fax: 886-3-3278211; E-mail: gerson@ms2.hinet.net

gliomas (grade 3 and 4 cerebral astrocytoma) consists of surgery and radiotherapy with median survival of 9 to 12 months.[1,2] However, despite tumor resection and radiotherapy, the disease recurs largely at the primary site. There are few long-term survivors.

The value of chemotherapy after standard postoperative external beam radiation in the treatment of malignant gliomas remains controversial. Several trials of chemotherapy combined with surgery and radiotherapy have shown only marginal benefits from the added drugs.[3-7] A meta-analysis of 16 randomized studies suggested that chemotherapy was advantageous for patients with malignant gliomas and should be considered part of the standard therapeutic regimen.[8] The most widely employed agents were the nitrosoureas (carmustine [BCNU] and lomustine [CCNU]). Nitrosoureas were shown to be promising and were considered as the most active agents. During the past decade, there has been considerable interest in using the combinations of BCNU and cisplatin or carboplatin to increase response rates.[9-11] Cisplatin was selected because of its definite, albeit low, activity against recurrent astrocytomas in phase II studies, its ability to concentrate in intracerebral tumors, and its radiosensitizing properties.[12] We reported on a combination of 72-hour infusions of BCNU and cisplatin administered before, during, and after cranial irradiation in 1995. However, this regimen resulted in moderate toxicity and there was a lack of apparent survival benefits compared with radiation therapy plus BCNU alone.[13] One team of researchers demonstrated that 72-hour infusions of BCNU and cisplatin followed by radiation did not improve survival and were associated with more serious toxicities than standard therapy.[14] A regimen using procarbazine, lomustine (CCNU), and vincristine (PCV) could be given as an outpatient treatment and was known to be of limited toxicity. Procarbazine had benefits similar to nitrosoureas when used in an adjuvant setting. Vincristine displayed some activity as a single agent against gliomas. The PCV regimen was considered the most effective combination chemotherapy with superiority over BCNU for anaplastic gliomas,[15] but a Medical Research Council (MRC) randomized trial showed no benefits to PCV chemotherapy.[16]

In an attempt to improve the survival of patients with high-grade astrocytomas, we researched a combination regimen program consisting of intravenous BCNU and cisplatin given as outpatient treatment concurrently with radiotherapy followed by PCV after radiotherapy.

METHODS

There were five eligibility requirements for patients in this study. The first requirement was a histologic diagnosis confirmed at surgery (subtotal or total tumor resection) or stereotactic biopsy, and tumors were classified as either anaplastic astrocytoma (AA) or glioblastoma multiforme (GBM). Each tumor was scored according to the presence or absence of the following four morphological criteria including: nuclear atypia, mitosis, endothelial proliferation, and necrosis. Each criterion was given a 0 or 1 score according to its presence or absence, and the cumulated score of the four items was translated into a grade as follows: 0 criterion = grade 1; 1 criterion = grade 2; 2 criteria = grade 3 (AA); and 3 or 4 criteria = grade 4 (GBM).[17] The second requirement was age below 75 years with good performance status (ECOG 0-2) and no previous chemotherapy or radiotherapy. The third requirement was the time from diagnosis to treatment must be less than 4 weeks with life expectancy of more than 6 weeks. The fourth requirement was normal complete blood count, platelet count, blood biochemistry, urinalysis, and prothrombin time. The fifth requirement was the absence of a psychiatric disorder.

The tumor resection was extended to the margin when clear appearance of gray-white matter was encountered under microscopic magnification, or under stereotactic localization guidance. The tumor resection at the functional cortex, such as motor, sensory, or language, was limited under the guidance of a somato-sensory evoked potentials cortical functional mapping technique. A gross excision might be obtained if the tumor did not encroach on the functional cortex.

After surgery, the chemotherapy protocol consisted of BCNU 100 mg/m^2 intravenous infusion for 2 hours every 4 weeks and cisplatin 50 mg/m^2 intravenous infusion for 3 hours every 2 weeks during the course of radiotherapy. The first cycle of the PCV regimen commenced 3 to 4 weeks after completion of radiotherapy. Each cycle involved procarbazine at 100 mg/m^2 orally on days 1 to 10, CCNU at 100

mg/m^2 orally on day 1, and vincristine at 1.5 mg/m^2 (maximum of 2 mg) intravenously on day 1. This was repeated every 6 weeks to a maximum of 4 cycles. Nausea and emesis were treated with metoclopramide, diphenhydramine, ondansetron, and dexamethasone. Corticosteroids were permitted in the minimal doses required to maintain the patient in an optimal neurologic condition. Anticonvulsants were used as medically indicated.

Radiation therapy was administered to patients on a 6 or 10 MV linear accelerator. Computerized radiation treatment planning was utilized in all cases. The treatment consisted of a single daily fraction of 180-200 cGy to the isocenter, either by opposed lateral whole brain portals or 3D conformal radiotherapy to the tumor bed with a 2-cm safety margin to a total dose 4000-5000 cGy, followed by a boost to the site of bulk disease with a limited margin to 6000-6500 cGy.

All patients in the study were evaluated initially by clinical and neurologic examinations and baseline cranial computed tomography (CT). All patients were followed up with neurologic examinations every 4 to 8 weeks and CT every 8 weeks. Time to tumor progression was measured from the date of surgery or biopsy to the date when the patient was determined to have progressive disease. Survival was measured from the date of surgery or biopsy to death or the last date of follow-up. The Kaplan-Meier production limit estimation method was used to estimate the survival times of different prognostic factors and a log rank test was used to detect the differences among them. Toxicities were monitored with a biweekly complete blood count and serum creatinine before each cycle of chemotherapy. When progressive disease was confirmed, patients were offered either additional surgery or chemotherapy according to their clinical status and the inclination of their primary care physicians.

RESULTS

From January 1994 through June 1998, 42 patients were enrolled in the study and treated at Chang Gung Memorial Hospital. The patient group consisted of 26 men and 16 women aged 17 to 74 years. Patient characteristics are listed in Table 1. All patients in the study were evaluated for toxicity to the combined therapy. The median number of cycles of BCNU and cisplatin was 2.5 (range, 1 to 3 cycles) and 4.5 (range, 2 to 6 cycles), respectively. The median number of cycles of PCV was 2.0 (range, 0 to 4 cycles). Eighteen (42%) patients received fewer than two cycles of PCV due to early deterioration of the patients' conditions and/or the refusal by the patients or their families to continue treatment. All 42 patients received radiotherapy. The total dose received ranged from 24 Gy to 68 Gy, with median dose at 60 Gy. Four of the patients (9.5%) had incomplete treatment because the accumulated dose was less than 50 Gy at the last visit for radiotherapy.

Table 1. Patient Characteristics, N=42

Characteristics	No. of patients (%)
Gender	
Male	26 (61.9%)
Female	16 (35.7%)
Median age in years	48.5 (range, 17-74)
Performance status (ECOG)	
0	2 (4.8%)
1	27 (64.3%)
2	13 (31.0%)
Histology	
Anaplastic astrocytoma	22 (52.4%)
Glioblastoma multiforme	20 (47.6%)
Locations of tumor	
Left hemisphere	18 (42.9%)
Right hemisphere	19 (45.2%)
Bilateral hemisphere	3 (7.1%)
Corpus callosum	1 (2.4%)
Suprasellar area	1 (2.4%)
Extent of neurosurgery	
Biopsy only	10 (23.8%)
Subtotal resection	19 (45.2%)
Total resection	13 (31.0%)
Median radiation dose	60 Gy (range, 24-68 Gy)

Abbreviation: ECOG: Eastern Cooperative Oncology Group.

The median follow-up time was 13.8 months (range, 1.7 to 108.2 months, as of May 31, 2003), and 37 deaths had been reported. The median time to progression was 7.2 months (range, 0 to 88.7 months). The median survival for the entire group of patients in the study was 13.3 months (range, 1.7 to 88.7 months) (Fig. 1). The median survival for four patients who received incomplete radiotherapy with dose less than 50 Gy was 5.1 months, compared to 15.1 months when dose more than 50 Gy was given (p=0.0094). The only factor that had a conventionally significant effect on overall survival was

resectability. Patients who received a subtotal/total resection had longer overall survival (18.0 months) compared with patients who received biopsy only (9.5 months; p=0.0031) (Fig. 2). The median survival time was 12.0 months for the patients with subtotal resection and 19.9 months for the patients with total resection. There was no evidence of survival differences between the two groups (p=0.387). The median survival time was 11.5 months for the patients with GBM and 15.7 months for the patients with AA. Again, there was no evidence of survival differences between these patients (p=0.2968).

Toxicity was evaluated using the World Health Organization (WHO) grading system. The maximum WHO grade over all cycles of chemotherapy received is listed in Table 2. All patients developed alopecia in the irradiated area; otherwise, the most common side effects were related to chemotherapy but not radiotherapy. Nausea and vomiting universally accompanied cisplatin infusion, but were successfully controlled with ondansetron and dexamethasone. Leukopenia was the major problem. Three patients required reduction in the dosage of BCNU and cisplatin. One patient developed peripheral neurotoxicity and hearing impairment after five cycles of cisplatin, and three patients had associated reversible nephrotoxicity. No treatment-related deaths occurred.

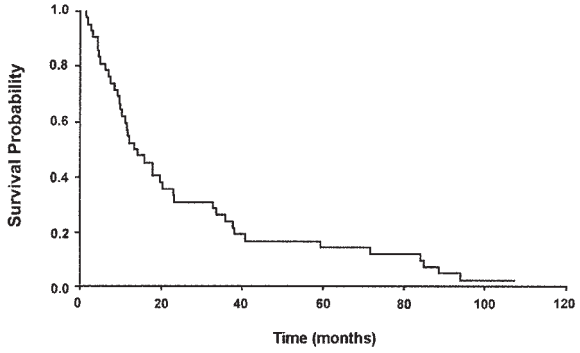

Fig. 1 Overall survival for all patients (N=42).

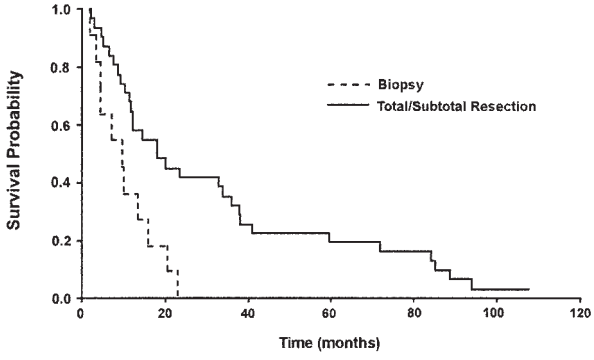

Fig. 2 Overall survival by extent of neurosurgery.

DISCUSSION

In this study, we reviewed 42 malignant glioma patients who were treated with BCNU and cisplatin during radiotherapy and PCV after radiotherapy. The median survival time was 13.3 months. The results did not disclose any obvious survival advantages as compared with previous treatment protocol.

The role of chemotherapy in addition to radiotherapy in the first-line treatment of supratentorial malignant gliomas remains controversial. A Brain Tumor Study Group (BTSG) study showed the combination of BCNU plus radiotherapy produced modest benefits in long-term (18-month) survival as compared with radiotherapy alone.[1,18] From the studies of various combinations of radiation therapy and adjuvant chemotherapy reported thus far, the standard treatment to which other therapies should be compared is still a single daily fraction irradiation to a total dose of 60 Gy plus adjuvant BCNU. The preliminary experience using BCNU and cisplatin presented by Grossman *et al*. for newly diagnosed cases of high-grade astrocytoma has shown this to be an exciting regimen.[9] However, the results of our previous study and an Eastern Cooperative Oncology Group (ECOG) trial using the same regimen failed to

Table 2. Maximal Chemotherapy Toxicity (according to WHO criteria), N=42

	No. of Patients				
	Grade				
Toxicity	0	1	2	3	4
Anemia	26	8	4	3	1
Neutropenia	26	2	7	5	2
Thrombocytopenia	28	7	3	3	1
Nausea/vomiting	21	6	8	5	2
Nephrotoxicity	39	3	0	0	0
Peripheral neurotoxicity	41	0	1	0	0
Ototoxicity	41	0	0	1	0

Abbreviation: WHO: World Health organization.

show increased survival benefits compared with radiation therapy plus BCNU alone.[13,14] Although the Northern California Oncology Group (NCOG) reported superiority of combination chemotherapy with PCV over BCNU alone in patients with AA,[15] there did not seem to be any survival benefits to PCV chemotherapy in recent trials.[16,19]

In our current study, we used the two potentially active regimens consisting of BCNU and cisplatin during radiotherapy and PCV after radiotherapy to treat patients with malignant gliomas. The study consisted of 42 evaluable patients and was a nonrandomized trial. The results of our study showed that the median time to progression of disease was 7.2 months and the median survival time was 13.3 months. The median survival of 13.3 months offered no substantial survival advantage over the median survival of patients who received conventional external-beam radiation therapy alone,[20] radiation therapy plus BCNU,[3] radiation therapy plus BCNU and cisplatin,[13,14] or radiation therapy plus PCV.[15,16]

We are unsure as to why our data showed no significant differences in the survival of AA and GBM patients. This was not consistent with other reports.[21] The relatively small sample size may be part of the explanation. In fact, patients with AA had a longer median survival time (15.7 months) than patients with GBM (11.5 months). It certainly points in a direction that is consistent with the experience of others. It is also important to emphasize that five of 10 patients (50.0%) who had biopsies only showed poor responses to the treatment, whereas only seven of 32 patients (21.9%) who had subtotal or total resection developed progressive disease within the first 4 months of therapy. The extent of the neurosurgery had an impact on overall survival. The statistically significant differences in survival between those who had biopsies only and those who underwent resection has already been well established. We are unsure as to why there were no significant survival differences between patients who had subtotal and total resections. The survival was 12.0 vs. 19.9 months for subtotal and total resection. The relatively small sample size in our series may be a part of the explanation. The data at least supports the theory that surgery with complete excisional intent is important as a debulking modality before aggressive treatment. The results also point out that minimal residual disease is more sensitive to radiotherapy.

Toxic effects associated with the combined agents of BCNU and cisplatin administered in conjunction with radiation therapy were mild to moderate. Leukopenia was the major problem. Three patients had elevated serum creatinine after five cycles of cisplatin. Ototoxicity from cisplatin occurred in one patient who received five cycles of cisplatin. The median number of cycles of PCV chemotherapy was two (range, 0 to 4 cycles). In general, the hematological toxicity of PCV was moderate, and in particular, there was no grade 3 or 4 neurotoxicity. Eighteen (42%) patients received less than two cycles of PCV due to early deterioration of the patients' conditions and/or refusal by the patients or their families to continue treatment.

The results of our trial indicated that there were no survival benefits to justify the increased costs and toxicities associated with these two potentially active regimens consisting of BCNU and cisplatin during radiotherapy and PCV after radiotherapy in patients with newly diagnosed malignant gliomas. Given the intensity of the BCNU, cisplatin, and PCV in this protocol, these findings make it unlikely that these agents can substantially affect this disease in an adjuvant setting. Furthermore, on the basis of these results, the likelihood of strategies using higher doses of standard chemotherapy with bone marrow or stem-cell rescue yielding positive results in the phase III context would be expected to be low.[14]

In conclusion, a combination of BCNU and cisplatin with cranial irradiation followed by PCV for malignant gliomas is moderately toxic and appears to offer no obvious survival advantages compared with radiotherapy plus BCNU and cisplatin or any other chemotherapy regimen. Before the results of novel agents such as temozolomide or irinotecan become available,[22,23] it is reasonable and appropriate not to offer routine adjuvant chemotherapy to individual patients until recurrence or participation in clinical trials.

REFERENCES

1. Walker MD, Alexander E Jr, Hunt WE, MacCarty CS, Mahaley MS Jr, Mealey J Jr, Norrell HA, Owens G, Ransohoff J, Wilson CB, Gehan EA, Strike TA. Evaluation of BCNU and/or radiotherapy in the treatment of anaplastic gliomas. A cooperative clinical trial. J Neurosurg 1978;49:333-43.
2. Kristiansen K, Hagen S, Kollevold T, Torvik A, Holme I,

Nesbakken R, Hatlevoll R, Lindgren M, Brun A, Lindgren S, Notter G, Andersen AP, Elgen K. Combined modality therapy of operated astrocytomas grade III and IV. Confirmation of the value of postoperative irradiation and lack of potentiation of bleomycin on survival time: a prospective multicenter trial of the Scandinavian Glioblastoma Study Group. Cancer 1981;47:649-52.
3. Walker MD, Green SB, Byar DP, Alexander E Jr, Batzdorf U, Brooks WH, Hunt WE, MacCarty CS, Mahaley MS Jr, Mealey J Jr, Owens G, Ransohoff J 2nd, Robertson JT, Shapiro WR, Smith KR Jr, Wilson CB, Strike TA. Randomized comparisons of radiotherapy and nitrosoureas for the treatment of malignant glioma after surgery. N Engl J Med 1980;303:1323-9.
4. EORTC Brain Tumor Group. Effect of CCNU on survival rate of objective remission and duration of free interval in patients with malignant brain glioma--final evaluation. E.O.R.T.C. Brain Tumor Group. Eur J Cancer 1978;14:851-6.
5. Chang CH, Horton J, Schoenfeld D, Salazer O, Perez-Tamayo R, Kramer S, Weinstein A, Nelson JS, Tsukada Y. Comparison of postoperative radiotherapy and combined postoperative radiotherapy and chemotherapy in the multidisciplinary management of malignant gliomas. A joint Radiation Therapy Oncology Group and Eastern Cooperative Oncology Group study. Cancer 1983;52:997-1007.
6. EORTC Brain Tumor Group. Evaluation of CCNU, VM-26 plus CCNU, and procarbazine in supratentorial brain gliomas. Final evaluation of a randomized study. European Organization for Research on Treatment of Cancer (EORTC) Brain Tumor Group. J Neurosurg 1981;55:27-31.
7. Edwards MS, Levin VA, Wilson CB. Brain tumor chemotherapy: an evaluation of agents in current use for phase II and III trials. Cancer Treat Rep 1980;64:1179-205.
8. Fine HA, Dear KB, Loeffler JS, Black PM, Canellos GP. Meta-analysis of radiation therapy with and without adjuvant chemotherapy for malignant gliomas in adults. Cancer 1993;71:2585-97.
9. Grossman SA, Wharam M, Sheidler V, Kleinberg L, Zeltzman M, Yue N, Piantadosi S. Phase II study of continuous infusion carmustine and cisplatin followed by cranial irradiation in adults with newly diagnosed high-grade astrocytoma. J Clin Oncol 1997;15:2596-603.
10. Kleinberg L, Grossman SA, Piantadosi S, Zeltzman M, Wharam M. The effects of sequential versus concurrent chemotherapy and radiotherapy on survival and toxicity in patients with newly diagnosed high-grade astrocytoma. Int J Radiat Oncol Biol Phys 1999;44:535-43.
11. Dazzi C, Cariello A, Giannini M, Del Duca M, Giovanis P, Fiorentini G, Leoni M, Rosti G, Turci D, Tienghi A, Vertogen B, Zumaglini F, De Giorgi U, Marangolo M. A sequential chemo-radiotherapeutic treatment for patients with malignant gliomas: A phase II pilot study. Anticancer Res 2000;20:515-8.
12. Stewart DJ, Leavens M, Maor M, Feun L, Luna M, Bonura J, Caprioli R, Loo TL, Benjamin RS. Human central nervous system distribution of cis-diamminedichloroplatinum and use as a radiosensitizer in malignant brain tumors. Cancer Res 1982;42:2474-9.
13. Kiu MC, Chang CN, Cheng WC, Lin TK, Wong CW, Tang SG, Leung WM, Chen LH, Ho YS, Ng KT. Combination chemotherapy with carmustine and cisplatin before, during, and after radiotherapy for adult malignant gliomas. J Neurooncol 1995;25:215-20.
14. Grossman SA, O'Neill A, Grunnet M, Mehta M, Pearlman JL, Wagner H, Gilbert M, Newton HB, Hellman R. Eastern Cooperative Oncology Group. Phase III study comparing three cycles of infusional carmustine and cisplatin followed by radiation therapy with radiation therapy and concurrent carmustine in patients with newly diagnosed supratentorial glioblastoma multiforme: Eastern Cooperative Oncology Group Trial 2394. J Clin Oncol 2003;21:1485-91.
15. Levin VA, Silver P, Hannigan J, Wara WM, Gutin PH, Davis RL, Wilson CB. Superiority of post-radiotherapy adjuvant chemotherapy with CCNU, procarbazine, and vincristine (PCV) over BCNU for anaplastic gliomas: NCOG 6G61 final report. Int J Radiat Oncol Biol Phys 1990;18:321-4.
16. Medical Research Council Brain Tumor Working Party. Randomized trial of procarbazine, lomustine, and vincristine in the adjuvant treatment of high-grade astrocytoma: a Medical Research Council trial. J Clin Oncol 2001;19:509-18.
17. Wang HC, Ho YS. Clinicopathological evaluation of 78 astrocytomas in Taiwan with emphasis on a simple grading system. J Neurooncol 1992;13:265-76.
18. Walker MD, Green SB, Byar DP, Alexander E Jr, Batzdorf U, Brooks WH, Hunt WE, MacCarty CS, Mahaley MS Jr, Mealey J Jr, Owens G, Ransohoff J 2nd, Robertson JT, Shapiro WR, Smith KR Jr, Wilson CB, Strike TA. Randomized comparisons of radiotherapy and nitrosoureas for the treatment of malignant glioma after surgery. N Engl J Med 1980;303:1323-9.
19. Prados MD, Scott C, Curran WJ Jr, Nelson DF, Leibel S, Kramer S. Procarbazine, lomustine, and vincristine (PCV) chemotherapy for anaplastic astrocytoma: A retrospective review of radiation therapy oncology group protocols comparing survival with carmustine or PCV adjuvant chemotherapy. J Clin Oncol 1999;17:3389-95.
20. Chang CN, Chen WC, Wei KC, Ng SH, Ho YS, Huang DY, Lee SP, Hong JH. High-dose-rate stereotactic brachytherapy for patients with newly diagnosed glioblastoma multiformes. J Neurooncol 2003;61:45-55.
21. Weller M, Muller B, Koch R, Bamberg M, Krauseneck P. Neuro-Oncology Working Group of the German Cancer Society. Neuro-Oncology Working Group 01 trial of nimustine plus teniposide versus nimustine plus cytarabine chemotherapy in addition to involved-field radiother-

apy in the first-line treatment of malignant glioma. J Clin Oncol 2003; 21:3276-84.
22. Stupp R, Newlands E. New approaches for temozolomide therapy: use in newly diagnosed glioma. Semin Oncol 2001;28 (4 Suppl 13):19-23.
23. Turner CD, Gururangan S, Eastwood J, Bottom K, Watral M, Beason R, McLendon RE, Friedman AH, Tourt-Uhlig S, Miller LL, Friedman HS. Phase II study of irinotecan (CPT-11) in children with high-risk malignant brain tumors: the Duke experience. Neuro-oncol 2002;4:102-8.

在carmustine和cisplatin複方化學療法之後給予procarbazine、lomustine和vincristine應用於成人高惡性度星狀細胞瘤的治療

廖繼鼎 魏國珍[1] 曾振淦[2] 容世明[3]

背 景：我們曾經報告過對高惡性度星狀細胞瘤病人在給予放射線療法的同時，併用BCNU和cisplatin對存活的改善不會優於只併用BCNU，而且產生更嚴重的毒性。爲了改善病人的存活，我們嘗試在併用BCNU和cisplatin之後再加上PCV。

方 法：從1994年1月到1998年6月這段期間，共有42位病人參與這個研究。其中有20位多形性神經膠質母細胞瘤和22位分化不良性星狀細胞瘤，中位年齡爲48.5歲。所有病人接受完全或部份腫瘤切除或組織切片做爲最初的步驟，之後，所有病人在給予放射線療法的同時，併用BCNU和cisplatin化學療法：BCNU每4週給予每平方公尺100毫克，cisplatin每2週給予每平方公尺50毫克。在放射線療法結束後的3到4週再開始給予每6週1次的PCV化學療法，最多給予4個療程：在每個療程的第1到10天每天給予procarbazine每平方公尺100毫克，在每個療程的第1天給予CCNU每平方公尺100毫克和給予vincristine每平方公尺1.5毫克（上限爲2毫克）。

結 果：中位追蹤期間是13.8個月（範圍：1.7至108.2個月）。手術後到腫瘤惡化是7.2個月（範圍：0至88.7個月）。中位存活期是13.3個月（範圍：1.7至88.7個月）。唯一對存活有意義的因子是可切除性，接受完全或部份腫瘤切除的病人比只接受組織切片的病人存活期較長（18.0和9.5個月, p=0.0031）。這個合併療法有10位病人發生第三級或第四級的血液毒性，1位病人發生第三級的聽力毒性，1位病人發生第二級的神經毒性。

結 論：在頭顱放射線照射的同時併用BCNU和cisplatin，在放射線照射之後再給予PCV產生中等度的毒性，加上PCV似乎對存活沒有明顯的幫助。

(長庚醫誌 2005;28:16-23)

關鍵字：化學療法，放射線療法，多形性神經膠質母細胞瘤，分化不良性星狀細胞瘤。

長庚紀念醫院　台北院區　血液腫瘤科，[1]腦神經外科，[2]放射腫瘤科，[3]病理科
受文日期：民國93年5月12日；接受刊載：民國93年11月18日。
索取抽印本處：廖繼鼎醫師，長庚紀念醫院　血液腫瘤科。桃園縣333龜山鄉復興街5號。Tel.: (03) 3281200轉2524; Fax: (03) 3278211; E-mail: gerson@ms2.hinet.net