Recurrent Multicentric Glioblastoma Multiforme Responds to Thalidomide and Chemotherapy

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Glioblastoma multiforme remains virtually incurable, with reported median survivals of less than 2 years with standard treatment.[1] In recent years, thalidomide (Thalomid) has shown activity in high-grade gliomas as a single agent and in combination with nitrosoureas and carboplatin (Paraplatin).[2-4] I will describe three cases in which patients with recurrent, multicentric glioblastoma responded to thalidomide plus chemotherapy after failing initial treatment with conventional radiation and chemotherapy for a single malignant glioma.

Case 1
A 43-year-old man diagnosed with anaplastic astrocytoma underwent a right frontal craniotomy and gross total resection in July 1998. The surgery was followed by external-beam radiation therapy and four cycles of cisplatin, etoposide, and vincristine. In December 1999, disease progression was found, and treatment was switched to single-agent temozolomide (Temodar). Disease continued to progress, and multiple enhancing lesions were documented in February 2000 (Figure 1). The patient then received six cycles of procarbazine (Matulane), lomustine (CCNU [CeeNu]), and vincristine in combination with daily thalidomide at a dose of 400 mg. Initial dose escalation of thalidomide to 600 mg/d was not well tolerated, and thereafter, the dose was maintained at 400 mg/d. Complete resolution of all lesions was observed after four cycles of therapy (see Figure 2, p 278).

Mild thrombocytopenia and leukopenia resolved upon completion of therapy with procarbazine, lomustine, and vincristine. Minor sensory peripheral neuropathy was noted but did not prevent the patient from working full time while receiving treatment. At 1½ years after disease recurrence, the patient continues to receive single-agent thalidomide.

Cases 2 and 3
Two other cases involving combination chemotherapy and thalidomide after failure of first-line therapy resulted in partial responses at our institution. In both cases, the patients were women with a history of breast cancer. Single brain lesions were initially suspected to be metastatic disease, but surgical resection identified them as primary anaplastic astrocytoma. These neoplasms did not respond to treatment with radiation therapy and temozolomide, and the disease progressed to multiple enhancing lesions in each patient, with a brain biopsy-confirmed diagnosis of glioblastoma multiforme.

Both patients subsequently received the combination of cisplatin, etoposide, and vincristine plus thalidomide (200 mg/d) and achieved partial responses (> 50% tumor reduction) after two cycles, with durable responses of 16 and 24 weeks. Escalation of the thalidomide dose to 400 mg/d was possible in one patient; the other was maintained at 200 mg/d after experiencing somnolence at higher doses. One patient died as a result of chemotherapy-induced thrombocytopenia, and the other died due to complications of meningeal carcinomatosis.

Conclusions
These cases suggest that the addition of thalidomide to standard chemotherapy regimens containing a nitrosourea, procarbazine, cisplatin, or etoposide may considerably enhance activity in patients with recurrent multicentric high-grade and malignant glioma. The implications of this preliminary experience in patients with a poor prognosis and few viable treatment options suggest that further study of thalidomide in combination with chemotherapy is warranted in this setting.

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