Response to Temozolomide in Supratentorial Multifocal Recurrence of Malignant Ependymoma

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Abstract. Intracranial anaplastic ependymomas are a very rare entity within the group of adult CNS neoplasms. Thus, no standard adjuvant therapy after surgical resection has been defined so far. External radiotherapy is commonly administered, but the role of chemotherapy is still unclear in malignant ependymomas. The case of a 25-year-old female patient with multifocal recurrence of a supratentorial malignant ependymoma administered temozolomide as second-line therapy is reported. Currently, 5 months after initiation of temozolomide treatment, there is no evidence of radiographic progression. Temozolomide could constitute a promising approach to supratentorial recurrent and multifocal anaplastic ependymoma of adults.

Intracranial anaplastic ependymomas are a rare entity within the group of neoplasms of neuroectodermal origin that arise from the ependymal cells of the cerebral ventricles and the choroid plexus (1). Only 2-8% of all primary CNS tumors are diagnosed as ependymomas, whereas just 11.5% of this group fulfill the criteria of malignancy. The mean age at diagnosis is 35 years, with a preponderance for males (2). Anaplastic (WHO˚III) ependymomas are characterized by local recurrence and distant multifocal metastatic spreading along cerebrospinal fluid pathways (2).

The treatment of ependymomas in general is gross total tumor resection leading to definite cure in 86% (3). In cases of anaplastic ependymoma there is no standard adjuvant treatment regime following surgical resection. Most of the published literature is not specifically focused on intracranial WHO˚III ependymomas. Recent publications favour gross total resection followed by radiation therapy (3, 4) as a standard treatment. Several chemotherapeutic agents have been described in case reports or small series (5-8) and consist of a widespread selection from carboplatin-based chemotherapy to intrathecal infusion of antineoplastic agents. In recurrent ependymoma, the therapeutic interventions are even more heterogeneous, with little or no efficacy (9) and high toxicity according to the National Cancer Institute Common Toxicity Criteria (9). Temozolomide has been used in recurrent ependymoma of WHO˚I and ˚II (10), and in recurrent childhood ependymoma of the posterior fossa (11).

Despite all reported treatment options, recurrence is a common feature (12). Generally, 38% of ependymomas in an adult population show recurrences, while high-grade ependymomas present with recurrent tumor in 72% of treated patients (3). In cases of diffuse infiltrating lesions or multifocal recurrence, the role of repeated surgical treatment or re-irradiation is limited. The impact of chemotherapy in recurrent anaplastic ependymomas is not yet clearly defined.

Case Report

In the present case, temozolomide was administered as a second-line therapy for a 25-year-old female who had tumor progression 5 months after primary microsurgical resection and adjuvant radiation therapy of a malignant ependymoma (Figure 1). At the time of progression, she presented with a multifocal recurrence. The dosage was calculated in relation to the body surface (with 150 mg/m²) and given for five days in a 28-day therapeutic cycle. A dramatic regression of the contrast-enhancing MRI lesion was observed after 12 weeks, indicating a remarkable response (Figure 2) without any evidence of treatment-related side-effects. Contrast enhancement further diminished on follow-up MRI. This was in parallel with the clinical symptoms.
Discussion

For malignant glioma, the standard adjuvant strategy is administration of concomitant and adjuvant temozolomide (13). The combination of radiation and temozolomide leads to a median overall survival of 14.6 months, with acceptable low rates of toxicity (13).

Although there is few data on prognosis, especially time to progression and overall survival, in recurrence of malignant ependymoma of adults, Green et al. (14) show a median time to progression of 4 months when treated with bevacizumab as second-line therapy, while Guyotat et al. describe a 0% five-year survival rate in intraparenchymatous anaplastic ependymoma, treated with platinum-based therapy in case of recurrence (15).

We report a case with an excellent response to temozolomide, indicating that temozolomide could be an effective and well-tolerated strategy for recurrence of malignant ependymoma following surgery and radiotherapy and might hold potential in the adjuvant setting, although further prospective investigations are necessary.

To our knowledge, this is the first report of an effective salvage treatment of multifocal intracranial malignant ependymoma with temozolomide, which could constitute a promising approach to supratentorial recurrent and multifocal anaplastic ependymoma of adults.

References


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