Chemotherapy for low-grade gliomas: when? how? how long?

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Low grade gliomas have remained to be among the most controversial brain tumors in many ways for decades. Their spontaneous behaviour as well as their response to therapy is difficult to predict, the outcome is highly variable. However, “low grade” sounds much more promising to a patient than “your expected median survival is 5-8 years”, especially if you are in your early thirties with lots of plans and obligations.

Standards of care are difficult to define for these tumors: subpopulations of patients certainly benefit from surgery, radiotherapy prolongs progression-free survival, and so does probably alkylating agent chemotherapy, too. For all therapeutic interventions, timing is also a controversial issue.

In this issue of *Neuro-Oncology*, Peyre and colleagues (1) report on the retrospectively determined time course of radiological responses to procarbacine+CCNU+vincristin (PCV) polychemotherapy in a series of 21 patients with low grade gliomas, predominantly oligodendroglial, who had not previously been treated with radiotherapy or other chemotherapy. Six cycles of PCV were intended to be given. Unexpectedly, the median tumor diameters of all patients decreased during PCV, more surprisingly even, they continued to decrease in 20 (1) of 21 for a median time of 2.7 years after cessation of PCV. According to their modified Macdonald criteria (2), the rates of partial and minor responses were 5% and 38% at the end of PCV but 38% and 42% at the time of maximal mean tumor diameter decrease, which occurred after a median period of 3.4 years after PCV onset.

While it is well recognized that response assessment in patients with low grade gliomas is challenging (3), the authors are to be commended for carefully assessing imaging changes over a fairly long follow-up. Nevertheless, it is almost astonishing that all of their 21 patients showed a reduction of mean tumor diameter on PCV. No data for a control group of patients treated with radiotherapy were presented. This would have helped to weigh these data against
a suggested benefit from PCV that may not correspond to everybody’s clinical experience with this regimen. Admittingly, of 21 patients, there were 15 oligodendrogliomas and 4 oligoastrocytomas.

That tumor sizes in general may shrink with a delay after the application of a cytotoxic or more likely genotoxic stimulus is clinically well recognized in irradiated tumors. Here it is often assumed that vasoocclusive, antiangiogenic effects are involved, e.g., when treating histologically benign lesions such as unresectable meningioma. Alternatively, Peyre et al. (1) propose that an altered balance between spontaneous cell death and proliferation might account for the delayed responses.

If accepted for radiotherapy, why should this not occur after delivery of a genotoxic signal via chemotherapy? Maybe this was just never looked at. Yet, a related group of authors from France previously analysed a similar group of low grade glioma patients who were treated with temozolomide (4). The dynamics of tumor growth were quite different: although 92% tumors responded initially, responses were often short-lasting despite continued treatment, and many tumors resumed growth early after the cessation of temozolomide. Importantly, the authors acknowledge the differential safety and tolerability of temozolomide versus PCV and refrain from treatment recommendations in favour of PCV based on this small, but impressive set of data.

References


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