
Low-grade gliomas have remained among the most controversial brain tumors, in many ways, for decades. Their spontaneous behavior, as well as their response to therapy, is difficult to predict, and their outcome is highly variable. Standards of care are difficult to define for these tumors: subpopulations of patients certainly benefit from surgery, and radiotherapy prolongs progression-free survival, as may alkylating-agent chemotherapy. 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 procarbazine + CCNU + vincristine (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 therapy; more surprisingly, they continued to decrease in 20 of the 21 cases for a median duration of 2.7 years after cessation of PCV therapy (1). According to their modified Macdonald criteria (2), the rates of partial and minor responses were 5% and 38% at the end of PCV therapy but 38% and 42% at the time of maximal mean tumor diameter decrease, which occurred a median of 3.4 years after PCV therapy 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 after PCV therapy. No data for a control group of patients treated with radiotherapy were presented. This would have helped to weigh these data against the suggested benefit from PCV therapy that may not correspond to everybody’s clinical experience with this regimen. Admittedly, of 21 patients, 15 had oligodendrogliomas, and 4 had oligoastrocytomas.

That tumor sizes in general may continue to shrink after the completion of a cytotoxic or more likely genotoxic stimulus is clinically recognized in irradiated tumors; it is often assumed that vasoocclusive, antiangiogenic effects are involved. Alternatively, Peyre et al. (1) propose that an altered balance between spontaneous cell death and proliferation might account for the delayed responses.

If this occurs with radiotherapy, why should it not occur after delivery of a genotoxic signal via chemotherapy? Maybe this has just never been evaluated. Yet a related group of authors from France previously analyzed a similar group of low-grade glioma patients who were treated with temozolomide (4). The dynamics of tumor growth were quite different: although 92% of 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 favor of PCV on the basis of this small but impressive set of data.

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References


