Editorial

Low-grade gliomas

M itchel S. Berger, M.D.

Department of Neurosurgery, University of California, San Francisco, California

The article by Capelle and colleagues,1 from the French Low-Grade Glioma Consortium, is a stellar example of “strength in numbers.” In essence, they have accumulated a significant number of patients with low-grade, that is, Grade II glial, neoplasms and assessed some of the “spontaneous prognostic factors” associated with outcome in this rather common type of glioma that confronts neurosurgeons on a daily basis. While many of their findings are not unusual or novel, the evidence provided by this large cohort of patients offers very convincing information concerning not only the natural history of this disease but also how patients with this diagnosis should be approached.

It has long been known and recognized that the size of a low-grade glioma is quite critical with regard to driving its biology. Indeed, this was one of the key criteria used in developing the University of California, San Francisco, low-grade glioma prognostic score, which was validated in their study2,5 and clearly affects the extent of resection. Tumor size also makes a very strong argument for why a “wait and see” approach to low-grade gliomas after their initial presentation is completely unacceptable in the modern era given our understanding of the natural history of this lesion. Other well-known prognostic factors, such as patient age, tumor location, and contrast enhancement, were confirmed in their study as well. It was somewhat surprising that histological phenotype did not influence outcome in this population, since we know that typically astrocytic gliomas do much worse than pure oligodendroglial tumors that have a 1p/19q codeletion.7 The other critically important factor influencing outcome has to do with a lesion location in eloquent areas. A previous report by our group demonstrated that patients with tumors presumed to be in eloquent locations and not surgically treated with the aid of intraoperative stimulation mapping fared much worse in terms of survival than patients with tumors presumed to be in eloquent areas but found not to be in eloquent areas based on intraoperative mapping.4 The reason for such a discrepancy in outcome related to eloquence and the use of functional mapping has to do with the extent of resection, which is significantly greater in an area that is mapped and found not to be eloquent despite presumably being located in functional tissue based on preoperative imaging studies. In fact, this is such a significant variable that an article recently appearing in the Journal of Clinical Oncology has described the impact of brain mapping on glioma outcome surgery in the form of a meta-analysis.6 This study clearly showed that there were fewer severe neurological deficits and more extensive resections in tumors within eloquent regions when brain mapping was used. Thus, it provides very strong evidence that mapping during surgery for gliomas in eloquent regions should become the standard of care.

Another critical issue has to do with how we as neurosurgeons can influence the outcome of this disease by being more surgically aggressive not only at the initial presentation but also at the time of recurrence. This large study, done in conjunction with the French Low-Grade Glioma Consortium, has shown once again that anaplastic transformation can be significantly delayed after a more aggressive resection, and thus change the natural history of the disease. The authors also demonstrated that the resection of recurrent low-grade gliomas significantly influenced survival in a multivariate analysis.2,7 As they point out, radiation and chemotherapy have a fairly minor role to play in this disease with regard to overall survival, leaving surgery and the extent of resection as the most important variables for predicting outcome in this tumor type.

Therefore, I think we have turned the corner as neurosurgeons and can no longer accept a wait-and-see attitude for any patient who presents with a low-grade glioma. With all of the surgical accouterments we have today, it is a rare circumstance that is truly inoperable, unless, of course, it involves gliomatosis cerebri or very deep-seated or multicentric lesions. We have the techniques available to us to perform aggressive radical resections very safely. And while the risk is certainly not zero in terms of surgical morbidity, the benefits significantly outweigh the risks, especially with regard to the most important outcomes, namely malignant transformation and overall survival. I want to commend the authors once more for an outstanding investigative study that again puts the onus on us as neurosurgeons to treat this disease in an aggressive fashion to give our patients the greatest chance possible to extend their lives while preserving its quality. (http://thejns.org/doi/abs/10.3171/2012.7.JNS121358)
Disclosure

The author reports no conflict of interest.

References


Response

LAURENT CAPELLE, M.D.,1 DENYS FONTAINE, M.D., PH.D.,2 EMMANUEL MANDONNET, M.D., PH.D.,3 LUC TAILLANDIER, M.D., PH.D.,4 LUC BAUCHET, M.D., PH.D.,5 JOHAN PALLUD, M.D.,6 AND HUGUES DUFFAU, M.D., PH.D.3

1Department of Neurosurgery, Groupe Hospitalier Pitié-Salpêtrière, Paris; 2Department of Neurosurgery, Centre Hospitalier Universitaire de Nice; 3Department of Neurosurgery, Hôpital Lariboisière, Paris; 4Departments of Neurology and Neurosurgery, Centre Hospitalier Universitaire de Nancy; 5Department of Neurosurgery, Centre Hospitalier Universitaire de Montpellier; and 6Department of Neurosurgery, Centre Hospitalier Sainte-Anne, Paris, France

We greatly thank Mitchel Berger, pioneer and leader in the field, for his editorial comments on our collaborative series of WHO Grade II gliomas in adults. Indeed, and hopefully, we were able to confirm in a significant number of cases the prognostic factors pertaining to the spontaneous history of these tumors, as well as to pinpoint once again the paramount importance of extensive resections when the patient and physicians agree on the goal to significantly delay, if not avoid, the ineluctable anaplastic transformation of the glioma, with its dismal prognosis.

The fact that histological phenotype did not significantly influence outcome in our series probably reflects changes in pathological views in the past decades and the interaction of various classifications in the pathologist’s mind. Nevertheless, the survival curves diverge more “classically” after 5–6 years of follow-up, separating oligodendroglial and astrocytic tumors. Moreover, the frequent existence within the tumor of astrocytic as well as oligodendroglial cells in various proportions, representing mixed gliomas that can behave as oligos, astros, or more intermediate tumors, might hamper clear (and statistical) distinctions. Progress in the fields of radiology and molecular biology is already enabling newer ways of glioma (prognostic and therapeutic) classification.

Extensive surgery in noneloquent and eloquent areas is indeed feasible with a low risk of additional morbidity and can be carried up to functional, not just oncological, limits thanks to intraoperative cortical and subcortical mapping. Statistically speaking, this treatment modality outperforms radio- and chemotherapy and must be proposed as the first-line option as well as for recurrences as much as possible. Even though chemo- and radiotherapy appear less effective in terms of survival, they do contribute to tumor control. They should probably be considered and used when possible as adjunctive therapies that can optimize resection. For example, the reduction of tumor extension on MRI by neoadjuvant chemotherapy can render possible or help to maximize a resection. The conjunction of these two treatments could result, in some cases at least, in a synergistic effect greater than the simple addition of both treatment modalities.

Hence, numerous clinical as well as fundamental research fields remain open, and we look forward to the progress that will be made in the next decades, if not the next years.

Please include this information when citing this paper: published online March 15, 2013; DOI: 10.3171/2012.7.JNS121358.