Low-Grade Gliomas

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This issue of *Neurosurgical Focus*, dedicated to low-grade gliomas, includes a review of oligodendrogliomas by Dr. Herbert Engelhard, who provides a comprehensive review of these unique tumors with respect to the diagnosis, treatment strategies, and molecular characteristics. In addition, Drs. Lopes and Laws present an extensive overview of the range of tumors that fall within the classification of low-grade lesions. Their work includes numerous illustrations that will serve as a wonderful resource for those not familiar with these tumors.

It is clear that the diagnosis of low-grade glioma is no longer sufficient to provide adequate information to direct treatment and to estimate outcome. Examination of recent evidence indicates that oligodendrogliomas and even oligoastrocytomas may be more susceptible to treatment than pure fibrillary astrocytomas. Additionally, there are a number of low-grade primary tumors that have an indolent course and do not require aggressive postsurgical treatment. It is important that the correct pathological diagnosis is recognized in these cases to reduce the risk of overtreatment and excessive morbidity.

The most common tumors, however, are fibrillary astrocytomas and oligodendrogliomas, and their optimum treatment regimen remains to be defined. There has been no randomized clinical trial to examine the role of surgery in determining outcome. The benefit of adjuvant radiotherapy also remains unproven. The issue regarding sensitivity to chemotherapy and the relationship with genetic markers (1p and 19q deletions) has been identified in anaplastic oligodendrogliomas and cannot be extrapolated to low-grade tumors.

The progression from a low-grade lesion to an anaplastic tumor is associated with specific clinical, radiological,

and pathological characteristics. Advanced patient age is clearly a poor prognostic indicator. In most publications the authors have used the age of 40 years as an arbitrary threshold, but the older the patient is, the worse the prognosis. Contrast enhancement in neuroimaging indicates neovascularization, and this appears to be a necessary precondition to anaplastic transformation. Increased tumor cell density, mitoses, and necrosis have proved to be less an indicator of a poor prognosis than when similar findings are present in an astrocytoma.

At our institution we have treated fibrillary astrocytomas and oligodendroglioma with aggressive resection when possible. Adjuvant therapy (radio- or chemotherapy) is generally withheld unless there is persistent symptomatic residual tumor. Because the presence of 1p deletions is less of a prognostic indicator in cases of low-grade lesions, we have not relied on this for adjuvant treatment-related decisions for nonanaplastic tumors; however, we are more likely to advocate chemotherapy prior to radiotherapy unless there is evidence of anaplastic transformation.

The lessons learned from the study of oligodendrogliomas serve as a paradigm for future research in neurooncology. It is likely that future therapy will rely on the molecular genetics that characterize specific gliomas in addition to the diagnostic classification of the entire morphology of tumor cells. This new classification strategy will likely result in identification of subclasses of tumors that may require different treatment regimens. What is most important is to identify how and why low-grade gliomas become high-grade tumors. Although the biological behavior of a low-grade glioma may be unpredictable, the outcome with a high-grade glioma is very predictable and consistently very poor.