

Natural history and surgical management of incidentally discovered low-grade gliomas

Clinical article

MATTHEW B. POTTS, M.D., JUSTIN S. SMITH, M.D., PH.D., ANNETTE M. MOLINARO, PH.D., AND MITCHEL S. BERGER, M.D.

Department of Neurological Surgery, Brain Tumor Research Center, University of California, San Francisco, California

Object. Low-grade gliomas (LGGs) are rarely diagnosed as an incidental, asymptomatic finding, and it is not known how the early surgical management of these tumors might affect outcome. The purpose of this study was to compare the outcomes of patients with incidental and symptomatic LGGs and determine any prognostic factors associated with those outcomes.

Methods. All patients treated by the lead author for an LGG incidentally discovered between 1999 and 2010 were retrospectively reviewed. "Incidental" was defined as a finding on imaging that was obtained for a reason not attributable to the glioma, such as trauma or headache. Primary outcomes included overall survival, progression-free survival (PFS), and malignant PFS. Patients with incidental LGGs were compared with a previously reported cohort of patients with symptomatic gliomas.

Results. Thirty-five patients with incidental LGGs were identified. The most common reasons for head imaging were headache not associated with mass effect (31.4%) and trauma (20%). Patients with incidental lesions had significantly lower preoperative tumor volumes than those with symptomatic lesions (20.2 vs 53.9 cm³, $p < 0.001$), were less likely to have tumors in eloquent locations (14.3% vs 61.9%, $p < 0.001$), and had a higher prevalence of females (57.1% vs 36%, $p = 0.02$). In addition, patients with incidental lesions were also more likely to undergo gross-total resection (60% vs 31.5%, $p = 0.001$) and had improved overall survival on Kaplan-Meier analysis ($p = 0.039$, Mantel-Cox test). Progression and malignant progression rates did not differ between the 2 groups. Univariate analysis identified pre- and postoperative volumes as well as the use of motor or language mapping as significant prognostic factors for PFS.

Conclusions. In this retrospective cohort of surgically managed LGGs, incidentally discovered lesions were associated with improved patient survival as compared with symptomatic LGGs, with acceptable surgical risks.

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KEY WORDS • glioma • low-grade glioma • asymptomatic • incidental • survival • oncology

PATIENTS with low-grade gliomas most commonly present with seizures.⁶ These lesions are rarely discovered as incidental findings during brain imaging for unrelated complaints or research studies.^{9,11,19,29,32} It is not clear how to best manage incidental asymptomatic LGGs, although some believe that there is no benefit to

early resection.^{2,18,23} However, a recent study has suggested that the surgical removal of incidental LGGs may in fact increase survival, possibly by allowing for a greater extent of resection.²⁰ We sought to verify these findings by examining our own experience with incidental LGGs treated using resection.

Abbreviations used in this paper: KPS = Karnofsky Performance Scale; LGG = low-grade glioma; MPFS = malignant progression-free survival; OS = overall survival; PFS = progression-free survival; SMA = supplementary motor area; ¹⁸F-FET = fluorine-18-labeled fluoroethyl-L-tyrosine.

Methods

The Committee on Human Research at the University of California, San Francisco, approved this study. We

identified adult patients (age ≥ 18 years) with an incidentally found hemispheric glioma who had undergone initial surgery (excluding diagnostic biopsy) performed by the lead author (M.S.B.) between 1999 and 2009. An “incidental” glioma was defined as a glioma found on imaging studies obtained for a reason unrelated to the underlying tumor such as trauma, headache without associated mass effect, or endocrinological workup. For patients presenting with headaches, we excluded those with signs of elevated intracranial pressure or those whose tumor demonstrated mass effect, as these factors could account for a headache. Medical records and pre- and postoperative imaging studies were reviewed in a retrospective fashion. Volumetric analysis of the tumor volume and extent of resection was performed using region of interest measurements of axial FLAIR sequences on pre- and postoperative MR imaging studies as previously described.²⁶ Extent of resection was calculated as follows: (preoperative tumor volume – postoperative tumor volume)/preoperative tumor volume.

Pathology review was based on WHO guidelines.¹⁵ Three outcome measures were assessed: OS, PFS, and MPFS. Overall survival was defined as the time from initial resection to death, with patients being censored at the time of the last follow-up of any kind (clinic visit or imaging). Death was based on a review of hospital records and the Social Security Death Index. Progression-free survival was defined as the time from initial resection to the demonstration of unequivocal tumor enlargement on follow-up imaging or death. Malignant PFS was defined as the time from initial resection to evidence of contrast-enhancement on follow-up MR imaging, higher-grade pathology from subsequent biopsy, or death. A comparison of incidental gliomas was made with symptomatic LGGs pulled from the cohort of LGGs described by Smith et al.²⁷ Preoperative and postoperative characteristics as well as outcome measures were obtained in an identical manner.

Statistical analysis was performed using both SPSS Statistics (IBM) and R (<http://www.r-project.org/>). Frequency distributions and summary statistics were calculated for all pre- and postoperative characteristic values. For categorical variables (that is, tumor location, pathological diagnosis, and so forth), cross-tabulations were generated, and chi-square or Fisher exact tests were used to compare their distributions between incidental and symptomatic patients. Additionally, logistic regression models were used for categorical variables with multiple levels. Continuous variables were compared using a t-test. Survival estimates (OS, PFS, and MPFS) were assessed with Kaplan-Meier curves and compared using the Mantel-Cox test. Univariate and multivariate analyses of factors associated with the primary outcomes among patients with incidental lesions were performed using Cox proportional hazards models.

For the 8 patients with serial imaging, the average slope of tumor growth (measured by tumor volume) was estimated using a linear mixed-effects model. As patients had varying tumor volumes at the time of diagnosis, a random intercept was included and the model was written as $y_{ij} = \beta_0 + \beta_1 t_{ij} + b_i + \varepsilon_{ij}$, where y_{ij} is the tumor vol-

ume for patient i at time of observation j , t_{ij} is the time of observation j for patient i , β_0 is the mean intercept, β_1 is the common slope or growth rate, b_i is the random effect parameter describing the shift in intercept for each patient, and ε represents the error. The model assumes ε is normally distributed with a mean 0 and variance σ^2 and that b_i follows a normal distribution with the mean 0 and variance/covariance matrix Ψ , which, because of the common growth rate, is a 1×1 matrix. The R Language and Environment for Statistical Computing and the NLME package were used for these computations.

Results

The lead author (M.S.B.) performed 364 first-time resections for newly diagnosed LGGs at his institution between 1997 and 2010. From this population, 35 patients (9.6%) met the study inclusion criteria. Baseline characteristics for these 35 patients are shown in Table 1. The mean age at discovery of the incidental lesion was 37.5 ± 1.8 years (mean \pm SEM). Headache was the most common reason for imaging leading to the diagnosis of glioma (11 [31.4%] of 35 patients), followed closely by trauma (7 [20%] of 35). Six patients presented with neurological signs, such as sensory symptoms, that did not localize to the site of the glioma. Headache descriptions by the 11 patients presenting with headaches included “migraine-like,” “low-grade,” or “throbbing.”

Eight patients (22.9%) underwent biopsy prior to referral to our institution. Pathology from biopsy samples revealed LGG in 6 patients and was inconclusive in 2. Based on preoperative pathology or imaging findings, the preoperative diagnosis was LGG in all 35 patients.

The mean time between discovery of the incidental lesion and resection was 10.4 ± 2.3 months. Twenty-four patients underwent resection within 6 months of discovery, while the remaining 11 patients were followed up with serial imaging for between 10 months and 4.3 years. Nine of these patients demonstrated lesion progression based on enlargement of the T2 FLAIR abnormality, ultimately prompting resection.

We had access to multiple preoperative MR images in 8 patients followed up with serial imaging for more than 1 year. Figure 1 left shows tumor volume versus time in these 8 patients, demonstrating essentially linear tumor growth over the time recorded with similar rates of growth for tumors of similar sizes. A linear mixed-effects model was utilized to estimate a common slope of $0.187 \text{ cm}^3/\text{month}$ (p value < 0.005). In Fig. 1 right we plotted each patient’s tumor volume against a volume-adjusted time, calculated as $t_{ij} = t_{ij} + b_i/\beta_1$. This aligns all growth curves along the average regression line that graphically accounts for differing times at diagnosis. We attempted a nonlinear mixed-effects model but were unable to get it to converge.

Comparing the patients who harbored incidental lesions with the cohort harboring symptomatic gliomas revealed several significant differences (Table 1). Patients with incidental lesions were more likely to be female (57.1% vs 36%, $p = 0.02$). They were also less likely to have eloquent tumor locations (14.3% vs 61.9%, $p <$

Incidental gliomas

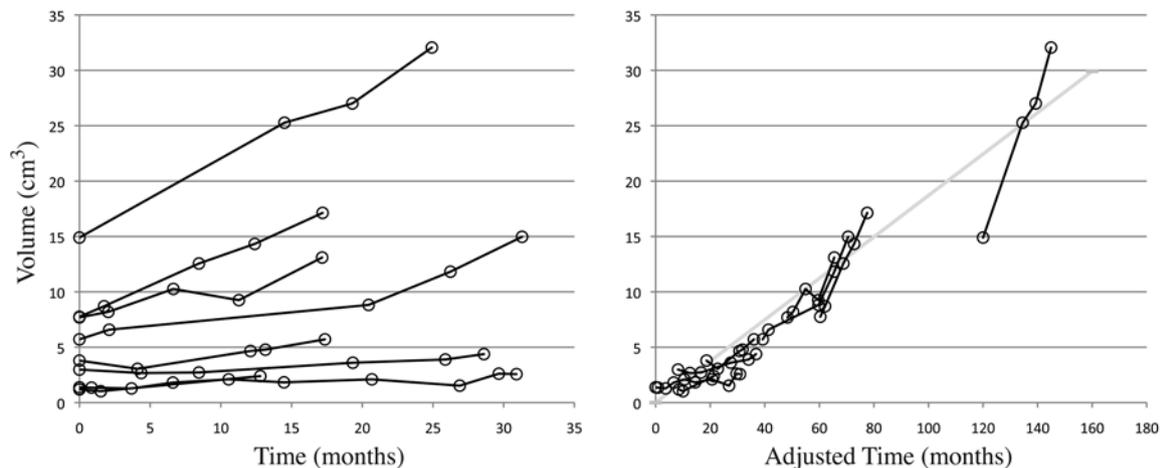


Fig. 1. Graphs showing tumor volumes of 8 patients with LGGs followed up with serial imaging prior to resection. Volumes are based on volumetric analysis. The common linear slope was calculated as $0.187 \text{ cm}^3/\text{month}$ according to a linear mixed-effects regression analysis ($p < 0.005$). **Left:** Volumetric growth for individual patients, with Time 0 defined as the first available MR imaging study. **Right:** Volumetric growth curves adjusted for times based on random intercepts and a common slope. Gray line represents the common linear slope.

0.001), with eloquence defined as a tumor involving the internal capsule; basal ganglia; language, sensory, or motor cortices; or hypothalamus. In addition, preoperative tumor volume was lower in patients with incidental lesions ($20.2 \text{ vs } 53.9 \text{ cm}^3$, $p < 0.001$). As expected, patients with incidental lesions had higher preoperative KPS scores ($p = 0.005$).

Intraoperatively, motor and speech mapping were performed in 19 (54.3%) and 10 (28.6%) patients, respectively. There was no intraoperative mortality. Operative results are presented in Table 2. Pathology revealed a Grade 1 ganglioglioma in 1 patient and Grade 2 gliomas (16 astrocytomas, 6 oligoastrocytomas, and 12 oligodendrogliomas) in the remaining 34 patients. The mean extent of resection was $95.7\% \pm 1.3\%$, with 21 patients (60%) having a gross-total resection. Comparing patients with incidental lesions to those with symptomatic lesions revealed a higher likelihood of gross-total resection (60% vs 31.5%, $p = 0.001$) as well as a greater mean extent of resection ($95.7\% \text{ vs } 77.1\%$, $p < 0.001$) and lower postoperative residual tumor volume ($1.1 \text{ vs } 17.2 \text{ cm}^3$, $p = 0.001$).

There were 3 recorded operative morbidities among patients with incidental lesions (8.6%). One patient with a left superior frontal gyrus glioma had postoperative aphonia that improved during the hospital stay but eventually required vocal cord collagen injections for persistent dysphonia. This patient had been intubated for the craniotomy, and it is believed that the complication was most likely associated with the intubation. A second patient with a left gyrus rectus glioma demonstrated acute aphasia on postoperative Day 1 and was found to have multiple small embolic infarcts on postoperative MR imaging. She recovered her neurological function completely, and a full workup of stroke risk factors was negative. The patient remained on daily aspirin at her last follow-up. A third patient with a left parietal glioma experienced Gerstmann syndrome postoperatively. This patient did not have any further clinical follow-up at our institution after discharge so it is not known if her neurological func-

tion improved. In addition, 3 patients with an expected postoperative SMA syndrome at the time of discharge subsequently recovered their neurological function. In comparison, 30 symptomatic patients (15.2%) had recorded postoperative neurological deficits. Of these, 26 attained complete recovery. In addition, 6 symptomatic patients had an expected postoperative SMA syndrome, which completely resolved in all.

The median postoperative duration of stay was 3 days, and the range was 2–7 days. Twenty patients were discharged with a KPS score of 100, whereas 10 had a KPS score of 90. The 3 patients with postoperative SMA syndromes were discharged with KPS scores of 50, 70, and 80, whereas the patient with postoperative Gerstmann syndrome had a KPS score of 80 at the time of discharge. One patient's discharge KPS score was not recorded.

The mean duration of follow-up was 5.1 years. Among the 35 patients with incidental lesions, there were 12 cases of progression (34.3%), 4 cases of malignant progression (11.4%), and 1 death (2.9%; Table 3). Three patients with progression became symptomatic with new-onset seizures or an increased seizure frequency, while a fourth exhibited new hemiplegia. The remaining patients had asymptomatic progression identified on serial imaging. Six patients underwent repeat resection, whereas the remaining patients were treated with a combination of temozolomide and/or radiation therapy. The diagnosis of malignant progression was based on pathology in 3 patients and new nodular enhancement on MR imaging in a fourth. The 1 patient who died was found to have malignant progression to glioblastoma multiforme on a repeat resection. After further progression on temozolomide therapy, this patient was treated with irinotecan and bevacizumab, but he continued to have progressive clinical deterioration in the setting of continued radiographic progression. He eventually elected hospice care. Survival analysis (Fig. 2) revealed significantly better OS in the incidental lesion group as compared with the symptomatic lesion group ($p = 0.039$, Mantel-Cox test). There were

TABLE 1: Summary of baseline characteristics in patients with LGG*

Parameter	Incidental Lesion	Symptomatic Lesion	p Value
no. of patients	35	197	
mean age at resection in yrs	38.4 ± 1.8	39.0 ± 0.7	0.73
no. of females (%)	20 (57.1)	71 (36)	0.02
no. of patients w/ symptom on presentation (%)			
headache	11 (31.4)	—	
trauma	7 (20)	—	
neurological change†	6 (17.1)	—	
hyperprolactinemia	3 (8.6)	—	
hearing loss	2 (5.7)	—	
infection	2 (5.7)	—	
other‡	4 (11.4)	—	
tumor location (%)			§
frontal	23 (65.7)	99 (50.3)	baseline
temporal	5 (14.3)	28 (14.2)	0.625
parietal	3 (8.6)	16 (8.1)	0.749
insular	4 (11.4)	54 (27.4)	0.044
lt-sided lesion (%)	20 (57.1)	108 (54.8)	0.8
eloquent tumor location¶	5 (14.3)	122 (61.9)	<0.001
% w/ contrast enhancement	5.7	9.1	0.75
mean tumor vol in cm ³	20.2 ± 2.9	53.9 ± 3.3	<0.001
preop KPS score (%)			**
100	27 (77.1)	90 (45.7)	baseline
90††	8 (22.9)	99 (50.3)	0.002
80	0	8 (4.1)	0.985
median time to resection in mos (range)	3.6 (1 mo–4.3 yrs)	NR	
previous biopsy (%)	8 (22.9)	NR	

* Values expressed as the means ± standard error, unless indicated otherwise. Abbreviations: NR = not recorded; — = not applicable.

† Neurological changes did not correlate with the location of the incidental tumor (for example, right-sided facial numbness with a right frontal lobe tumor).

‡ Includes 1 patient with a family history of aneurysms who underwent MR imaging for screening, 1 who was being worked up for a positive antinuclear antibody syndrome, 1 with periorbital edema, and 1 patient whose exact presentation is unknown but whose records stated “incidental.”

§ Logistic regression model with frontal lobe defined as baseline. Insular location was more likely in the symptomatic group with an OR of 3.13 compared to frontal lobe ($p = 0.044$).

¶ Defined as internal capsule, basal ganglia, language cortex, sensory cortex, motor cortex, or hypothalamus.

** Logistic regression model with KPS score 100 defined as baseline. A KPS score of 90 was more likely in the symptomatic group ($p = 0.002$).

†† All patients with a preoperative KPS score of 90 in the incidental group presented with either headaches (6) or hearing loss (2).

no significant differences in PFS or MPFS between the 2 groups ($p = 0.633$ and 0.55 , respectively).

Univariate analysis was performed to identify possible prognostic factors of outcome among patients with incidental LGG. Variables tested included age, sex, time to resection, tumor site, eloquence of tumor location, volume, enhancement, KPS score, use of intraoperative mapping, pathology, extent of resection, and use of adjuvant therapy. Due to the small number of deaths and malignant progressions, meaningful univariate analysis could only be performed for PFS. Preoperative and postoperative

volumes were associated with PFS (hazard ratios of 1.037 [$p = 0.059$] and 1.167 [$p = 0.093$], respectively, for a 1-cm³ increase in tumor volume). In addition, the use of intraoperative motor or speech mapping was also associated with PFS (hazard ratio 3.26, $p = 0.079$). When multivariate analysis was performed including these 3 factors, all 3 lost significance.

Discussion

Incidental LGGs are rare, and thus, their natural his-

Incidental gliomas

TABLE 2: Postoperative diagnosis and outcome*

Parameter	Incidental Lesion	Symptomatic Lesion	p Value
no. of patients	35	197	
postop diagnosis (%)			†
ganglioglioma	1 (2.9)	0	0.985
Grade 2 astrocytoma	16 (45.7)	81 (41.1)	baseline
Grade 2 oligoastrocytoma	6 (17.1)	30 (15.2)	0.981
Grade 2 oligodendroglioma	12 (34.3)	86 (43.7)	0.399
patients w/ gross-total resection (%)	21 (60)	62 (31.5)	0.001
overall mean extent of resection (%)	95.7 ± 1.3	77.1 ± 1.8	<0.001
overall mean residual tumor vol (cm ³)	1.1 ± 0.4	17.2 ± 1.9	0.001
mean extent of resection in STR (%)‡	89.2 ± 2.4	66.5 ± 2.3	0.001
residual vol in STR (cm ³)‡	2.8 ± 0.7	25.1 ± 2.5	0.006
mean duration of follow-up (yrs)	5.1 ± 0.6	5.0 ± 0.2	0.95

* Values expressed as the means ± standard error of the mean. Abbreviation: STR = subtotal resection.

† Logistic regression model with Grade 2 astrocytoma defined as baseline.

‡ In patients with subtotal resection: incidental lesion, 14 patients; symptomatic lesion, 135 patients.

tory prior to symptomatic onset is poorly understood. In addition, the appropriate management of incidental LGG is controversial, with only recent evidence indicating that early surgical treatment may offer a survival benefit.²⁰ Here, we presented our experience with 35 patients harboring incidental LGGs that were surgically managed. We showed that incidental gliomas are a distinct population from their symptomatic counterparts in that they are smaller and less likely to occur in eloquent locations. They are also associated with a greater extent of resection and better subsequent OS.

Incidental LGGs have been reported largely in brain imaging studies of healthy volunteers with incidences ranging from 0.025% to 0.3%.^{9,11,17,19,29} In a series of over 5000 gliomas from the French Brain Tumor Databank, 3% were reported as asymptomatic at the time of discov-

ery.¹ While some authors have studied patients with LGG followed up via observation,^{23,24} we have identified only 1 prior study that specifically focused on long-term outcomes in patients with incidental LGGs. Pallud et al.²⁰ reported on 47 patients with incidental LGGs and compared them to more than 1200 patients with LGGs from the French glioma study group. Their findings agreed with ours in that the patients harboring incidental LGGs had smaller tumors in noneloquent locations and were more likely to attain gross-total resection as compared with the patients harboring symptomatic lesions. Overall survival was also better in patients with incidental lesions. Pallud and colleagues also found that the patients with incidental gliomas were younger and less likely to have contrast-enhancing lesions than were those with symptomatic gliomas—variables that were not significantly different

TABLE 3: Characteristics of patients with postoperative tumor progression

Case No.	Age (yrs)	Time to Resection (mos)	Initial Pathology	Preop Tumor Vol (cm ³)	Extent of Resection (%)	Residual Tumor Vol (cm ³)	Postop Treatment	Time to Progression (yrs)	Repeat Resection	Malignant Progression*
1	33.3	4.6	astrocytoma	28.5	100	0	none	1.1	yes	no
2	36.2	1.8	oligoastrocytoma	6.75	90.6	0.6	none	0.5	no	no
3	34.6	1.7	oligoastrocytoma	23.11	95.3	1.1	none	4.5	no	no
4	24.4	0.9	astrocytoma	9.6	100	0	none	2.3	yes	no
5	33.9	2.1	oligodendroglioma	30.0	100	0	none	5.8	yes	yes
6	38.5	2.1	astrocytoma	34.1	91.9	2.8	none	0.4	no	yes
7	28.5	4.3	astrocytoma	63.1	89.9	6.4	none	1.1	yes	yes
8	24.7	24.8	astrocytoma	32.1	74.5	8.2	temozolomide	5.6	yes	yes
9	44.9	30.1	oligodendroglioma	3.4	100	0	none	1.8	yes	no
10	54.1	17.4	oligodendroglioma	5.7	100	0	none	2.5	no	no
11	44.3	0.9	astrocytoma	45.9	100	0	none	4.3	no	no
12	31.4	39.4	astrocytoma	31.2	81.2	5.9	none	4	no	no

* Based on repeat biopsy or MR imaging findings (presence of new enhancement).

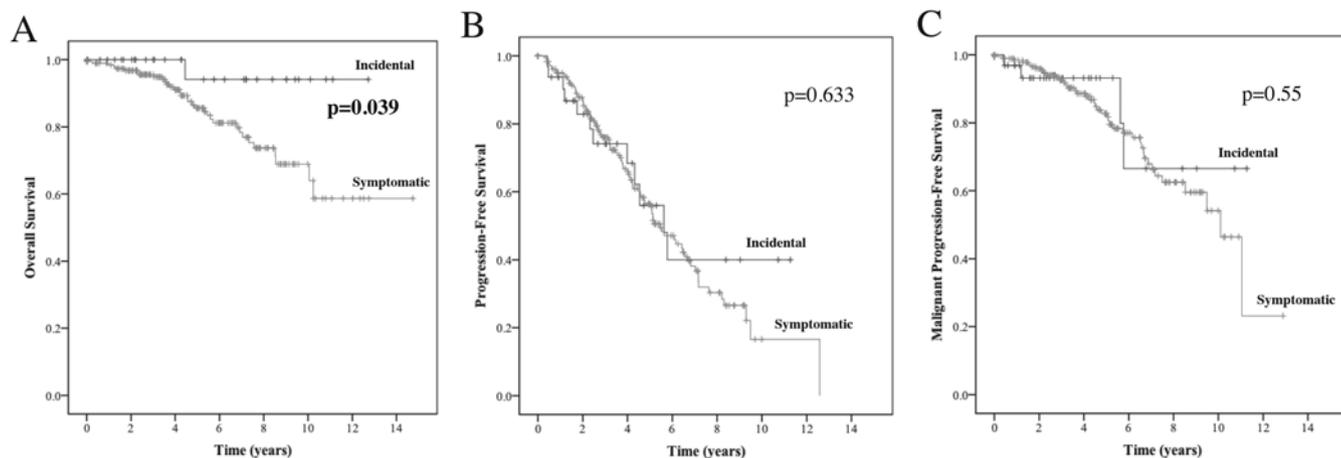


Fig. 2. Kaplan-Meier survival curves for OS, PFS, and MPFS. Each curve compares patients harboring incidental LGGs with those harboring symptomatic LGGs. **A:** Overall survival ($p = 0.039$, log-rank test). **B:** Progression-free survival ($p = 0.633$, log-rank test). **C:** Malignant PFS ($p = 0.55$, log-rank test).

between our own incidental and symptomatic cohorts. Interestingly, several patients were observed until their tumors became symptomatic, which occurred an average of 48 months after discovery. No patient treated with a “wait-and-watch” strategy in our series was monitored until the onset of symptoms. Instead, the decision to proceed with resection was typically made when significant tumor growth was noted on serial imaging.

The natural growth rate of LGGs is believed to be linear with regard to diameter and to progress at an average rate of around 4 mm/year.^{8,16,28,31} There is some variability to this rate, however, with faster tumor growth correlating with poorer outcomes.²¹ The growth rate of gliomas is thought to represent the migration of tumor cells as well as their proliferation.²⁸ With volumetric analysis, we demonstrated linear volumetric growth with a common slope of 0.187 cm³/month. Based on a prior demonstration of linear diametric expansion, we would expect exponential volumetric growth, but we were unable to obtain convergence of a nonlinear mixed-effect model. With a larger number of patients and longer observation time, we would probably be able to estimate patient-specific slopes as well as nonlinear effects.

Low-grade gliomas are most commonly diagnosed in males,⁴ but we found that there was a predominance of females among our incidental series. Pallud et al.²⁰ reported a similar finding in their series of incidental gliomas and postulated that it was attributable to a higher incidence of headaches in women. The converse argument could be made that men are more likely to be evaluated for traumatic brain injury.¹³ In our series, women were more likely than men to present with headaches (40% of women vs 20% of men), whereas men were more likely to present with trauma (40% of men vs 5% of women). Overall, however, women are more likely than men to seek medical care,³ which probably accounts for the higher incidence of incidental LGGs in women.

In addition to the female predominance, we showed that incidental tumors are smaller and less likely to occur in eloquent locations. The KPS score was also higher in patients with incidental lesions than in those harboring

symptomatic lesions. These findings are not surprising and concur with the findings of Pallud et al.²⁰ Importantly, it is likely these same factors lead to the better outcomes seen among the patients with incidental lesions in our series, both in terms of extent of resection and OS. Tumor volume, tumor location, and preoperative KPS score have all been identified as significant prognostic factors in LGG outcome.^{5,7,12,14,22,25,27,30} Tumor volume was also associated with a greater extent of resection, which in turn was associated with OS, PFS, and MPFS.²⁷ While prior studies have suggested that the timing of surgical management in incidental or minimally symptomatic LGGs may not affect overall outcome,^{2,23} the data presented here suggest that the finding of an incidental LGG provides the opportunity for resection when the tumor is at its smallest, facilitating the greatest extent of resection possible for a given patient. Among patients with incidental lesions, we identified pre- and postoperative tumor volume and the use of intraoperative mapping as prognostic factors for PFS in a univariate analysis. The effects of these factors are likely intertwined but lost significance in a subsequent multivariate analysis—most likely because of the small number of patients with incidental lesions, but we must consider the possibility that these factors have no real effect on this population. A larger cohort of patients with incidental lesions may be required to further characterize the prognostic factors.

Management options for an incidental finding suspicious for LGG typically include observation, biopsy, or resection. The end points of observation can involve the detection of tumor growth or the onset of symptoms. Floeth et al.¹⁰ provided evidence to suggest that gliomas can be diagnosed based on tumor growth demonstrated on serial imaging. They prospectively followed 21 patients with small (< 10 cm³), supratentorial, nonenhancing, and T2 hyperintense lesions that were found incidentally. They recorded tumor growth and ¹⁸F-FET PET results. Two patients had lesions that demonstrated slow growth and negative ¹⁸F-FET PET studies. Subsequent tissue revealed WHO Grade 2 astrocytomas. A second group of patients had rapid growth with positive ¹⁸F-FET PET

findings and were found to have high-grade gliomas. Two additional groups of patients had MR imaging lesions that either completely regressed or remained stable and were not biopsied. While the outcomes of these patients with incidental lesions were not reported, this study demonstrates the difficulty in managing incidental lesions given that the diagnosis of LGG is not always certain. It is possible that a short course of observation may be sufficient to detect tumor growth. Waiting for symptomatic onset, however, runs the risk of a patient experiencing seizures or presenting for resection with a lower KPS score.

Conclusions

The potential risks and benefits of resection must always be carefully considered, especially when a patient is asymptomatic. Here, we showed that surgical morbidity is actually lower in patients with incidental lesions, which is probably related to the higher preoperative functional status seen in patients with incidental lesions as well as the noneloquent location of the incidental LGGs. Overall, this study provides further data that the surgical management of incidental LGGs is safe and may be associated with better outcomes as compared with symptomatic LGGs. The data argue that resection, as opposed to a watch-and-wait strategy, should be offered to patients with incidental LGGs.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Potts, Berger. Acquisition of data: Potts, Smith. Analysis and interpretation of data: Potts. Drafting the article: Potts. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Potts. Statistical analysis: Molinaro. Study supervision: Berger.

References

- Bauchet L, Rigau V, Mathieu-Daudé H, Figarella-Branger D, Hugues D, Palusseau L, et al: French brain tumor data bank: methodology and first results on 10,000 cases. *J Neurooncol* **84**:189–199, 2007
- Cavaliere R, Lopes MB, Schiff D: Low-grade gliomas: an update on pathology and therapy. *Lancet Neurol* **4**:760–770, 2005
- Centers for Disease Control and Prevention: **National Ambulatory Medical Care Survey: 2008 Summary Tables**. (http://www.cdc.gov/nchs/data/ahcd/names_summary/namcssum2008.pdf) [Accessed September 19, 2011]
- Central Brain Tumor Registry of the United States: **CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2004–2005**. (<http://www.cbtrus.org/reports/2009-NPCR-04-05/CBTRUS-NPCR2004-2005-Report-.pdf>) [Accessed September 19, 2011]
- Chang EF, Clark A, Jensen RL, Bernstein M, Guha A, Carabba G, et al: Multiinstitutional validation of the University of California at San Francisco Low-Grade Glioma Prognostic Scoring System. Clinical article. *J Neurosurg* **111**:203–210, 2009
- Chang EF, Potts MB, Keles GE, Lamborn KR, Chang SM, Barbaro NM, et al: Seizure characteristics and control following resection in 332 patients with low-grade gliomas. *J Neurosurg* **108**:227–235, 2008
- Chang EF, Smith JS, Chang SM, Lamborn KR, Prados MD, Butowski N, et al: Preoperative prognostic classification system for hemispheric low-grade gliomas in adults. Clinical article. *J Neurosurg* **109**:817–824, 2008
- Duffau H, Pallud J, Mandonnet E: Evidence for the genesis of WHO grade II glioma in an asymptomatic young adult using repeated MRIs. *Acta Neurochir (Wien)* **153**:473–477, 2011
- Eskandary H, Sabba M, Khajehpour F, Eskandari M: Incidental findings in brain computed tomography scans of 3000 head trauma patients. *Surg Neurol* **63**:550–553, 2005
- Floeth FW, Sabel M, Stoffels G, Pauleit D, Hamacher K, Steiger HJ, et al: Prognostic value of 18F-fluoroethyl-L-tyrosine PET and MRI in small nonspecific incidental brain lesions. *J Nucl Med* **49**:730–737, 2008
- Katzman GL, Dagher AP, Patronas NJ: Incidental findings on brain magnetic resonance imaging from 1000 asymptomatic volunteers. *JAMA* **282**:36–39, 1999
- Kreth FW, Faist M, Rossner R, Volk B, Ostertag CB: Supratentorial World Health Organization Grade 2 astrocytomas and oligoastrocytomas. A new pattern of prognostic factors. *Cancer* **79**:370–379, 1997
- Langlois JA, Rutland-Brown W, Thomas KE: **Traumatic Brain Injury in the United States: Emergency Department Visits, Hospitalizations, and Deaths**. Atlanta: Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, 2006 (http://www.cdc.gov/ncipc/pub-res/tbi_in_us_04/tbi%20in%20the%20us_jan_2006.pdf) [Accessed September 19, 2011]
- Leighton C, Fisher B, Bauman G, Depiero S, Stitt L, MacDonald D, et al: Supratentorial low-grade glioma in adults: an analysis of prognostic factors and timing of radiation. *J Clin Oncol* **15**:1294–1301, 1997
- Louis DN, Ohgaki H, Wiestler OD, Cavenee WK: **WHO Classification of Tumours of the Central Nervous System, ed 4**. Lyon: IARC Press, 2007
- Mandonnet E, Delattre JY, Tanguy ML, Swanson KR, Carpentier AF, Duffau H, et al: Continuous growth of mean tumor diameter in a subset of grade II gliomas. *Ann Neurol* **53**:524–528, 2003
- Morris Z, Whiteley WN, Longstreth WT Jr, Weber F, Lee YC, Tsushima Y, et al: Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis. *BMJ* **339**:b3016, 2009
- Olson JD, Riedel E, DeAngelis LM: Long-term outcome of low-grade oligodendroglioma and mixed glioma. *Neurology* **54**:1442–1448, 2000
- Onizuka M, Suyama K, Shibayama A, Hiura T, Horie N, Miyazaki H: Asymptomatic brain tumor detected at brain check-up. *Neurol Med Chir (Tokyo)* **41**:431–435, 2001
- Pallud J, Fontaine D, Duffau H, Mandonnet E, Sanai N, Taillandier L, et al: Natural history of incidental World Health Organization grade II gliomas. *Ann Neurol* **68**:727–733, 2010
- Pallud J, Mandonnet E, Duffau H, Kujas M, Guillemin R, Galanaud D, et al: Prognostic value of initial magnetic resonance imaging growth rates for World Health Organization grade II gliomas. *Ann Neurol* **60**:380–383, 2006
- Pignatti F, van den Bent M, Curran D, Debruyne C, Sylvester R, Therasse P, et al: Prognostic factors for survival in adult patients with cerebral low-grade glioma. *J Clin Oncol* **20**:2076–2084, 2002
- Recht LD, Lew R, Smith TW: Suspected low-grade glioma: is deferring treatment safe? *Ann Neurol* **31**:431–436, 1992
- Rees J, Watt H, Jäger HR, Benton C, Tozer D, Tofts P, et al:

- Volumes and growth rates of untreated adult low-grade gliomas indicate risk of early malignant transformation. **Eur J Radiol** **72**:54–64, 2009
25. Schomas DA, Laack NN, Rao RD, Meyer FB, Shaw EG, O'Neill BP, et al: Intracranial low-grade gliomas in adults: 30-year experience with long-term follow-up at Mayo Clinic. **Neuro-oncol** **11**:437–445, 2009
 26. Smith JS, Cha S, Mayo MC, McDermott MW, Parsa AT, Chang SM, et al: Serial diffusion-weighted magnetic resonance imaging in cases of glioma: distinguishing tumor recurrence from postresection injury. **J Neurosurg** **103**:428–438, 2005
 27. Smith JS, Chang EF, Lamborn KR, Chang SM, Prados MD, Cha S, et al: Role of extent of resection in the long-term outcome of low-grade hemispheric gliomas. **J Clin Oncol** **26**:1338–1345, 2008
 28. Swanson KR, Bridge C, Murray JD, Alvord EC Jr: Virtual and real brain tumors: using mathematical modeling to quantify glioma growth and invasion. **J Neurol Sci** **216**:1–10, 2003
 29. Weber F, Knopf H: Incidental findings in magnetic resonance imaging of the brains of healthy young men. **J Neurol Sci** **240**:81–84, 2006
 30. Wessels PH, Weber WE, Raven G, Ramaekers FC, Hopman AH, Twijnstra A: Supratentorial grade II astrocytoma: biological features and clinical course. **Lancet Neurol** **2**:395–403, 2003
 31. Woodward DE, Cook J, Tracqui P, Cruywagen GC, Murray JD, Alvord EC Jr: A mathematical model of glioma growth: the effect of extent of surgical resection. **Cell Prolif** **29**:269–288, 1996
 32. Yue NC, Longstreth WT Jr, Elster AD, Jungreis CA, O'Leary DH, Poirier VC: Clinically serious abnormalities found incidentally at MR imaging of the brain: data from the Cardiovascular Health Study. **Radiology** **202**:41–46, 1997

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Address correspondence to: Matthew B. Potts, M.D., 505 Parnassus Avenue, M779, San Francisco, California 94143-0112. email: pottsm@neurosurg.ucsf.edu.