Indications for surgery in patients with asymptomatic meningiomas based on an extensive experience

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Object. To determine the indications for surgery in patients harboring asymptomatic meningiomas, the authors retrospectively analyzed the natural course and surgical outcome of asymptomatic meningiomas and then compared these to the natural course and surgical outcome of symptomatic meningiomas.

Methods. Between 1989 and 2003, 1434 patients harboring meningiomas, who were treated in Kumamoto Prefecture, Japan, were enrolled in this study. Six hundred three patients had asymptomatic lesions and 831 had symptomatic ones. The authors analyzed the sizes of the lesions at detection, their growth over time, and any appearances of symptoms associated with previously asymptomatic meningiomas. The authors then compared the surgery-related morbidity rates associated with asymptomatic and symptomatic meningiomas arising at different locations.

Of the 603 asymptomatic meningiomas, 351 (58.2%) were treated conservatively. Tumor growth was observed in 25 (37.3%) of 67 patients who participated in follow up for longer than 5 years, and symptoms developed in 11 (16.4%) of the 67 patients over a mean follow-up period of 3.9 years. Among the 213 patients with surgically treated asymptomatic meningiomas, the morbidity rate was 4.4% in patients younger than 70 years of age and 9.4% in those 70 years of age or older. Although the total morbidity rate was lower in patients with asymptomatic lesions than in those with symptomatic ones, it exceeded 6% in patients whose asymptomatic tumors were located at the convexity or falx.

Conclusions. Approximately 63% of asymptomatic meningiomas did not exhibit tumor growth, and only 6% of all patients with these lesions experienced symptoms during the observation period. To avoid surgery-related incidences of morbidity in patients with asymptomatic meningiomas, conservative treatment with close follow-up review may be the best therapeutic strategy.

Key Words • meningioma • surgery • natural course of disease

The increase in elderly persons in the general population and advances in diagnostic techniques and instrumentation have led to an increase in the detection of asymptomatic meningiomas. At autopsy, Nakasu and colleagues found that 2.3% of all cadavers and 3% of cadavers of persons who were older than 60 years at the time of death harbored meningiomas. Using neuroimaging as a diagnostic tool, Kuratsu et al. calculated the incidence rate of asymptomatic meningiomas per 100,000 population per year in Kumamoto to be 1.19. Not only neurosurgeons, but also their patients, must decide whether and how to treat these asymptomatic meningiomas. To assess the indications for surgery in patients with asymptomatic meningiomas, we posed the following questions: 1) What is the tumor growth rate? 2) How many asymptomatic tumors eventually become symptomatic? 3) If patients with asymptomatic tumors undergo surgery, is the incidence of morbidity lower than that in surgically treated symptomatic patients? To investigate these questions, we conducted a retrospective study of 1434 patients with meningiomas who had been treated in Kumamoto Prefecture, Japan, and attempted to develop a strategy for treating patients with asymptomatic meningiomas.

Clinical Material and Methods

Patient Population

Data on residents of Kumamoto Prefecture, Japan, with a diagnosis of meningioma were obtained from the Kumamoto University Brain Tumor Data Bank, which includes information on almost all patients with primary intracranial tumors that were diagnosed between 1989 and 2003 (see Appendix for all hospitals contributing information to this database). Records were available on age and sex, date of diagnosis, and treatment in all patients, including those who were still participating in follow up. For our retrospective study, we conducted a review of the hospital records and imaging studies available in September 2004. The imaging-based diagnosis of meningioma was determined on the presence of a mass located in the extraaxial dura mater that was uniformly and markedly contrast enhanced. The size of the tumor was determined by measuring its largest diameter, and its growth was calculated as any measurable increase in this diameter. Associated instances of morbidity, whether medically related (for example, pneumonia, pulmonary in-

Abbreviation used in this paper: MR = magnetic resonance.
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fashion, angina, and deep vein thrombosis), surgery related
(for example, wound infection, intracerebral bleeding, sub-
cutaneous fluid collection, and brain swelling), or neurolog-
ically related (for example, paresis, numbness, visual distur-
bance, and other neurological deficits) that present within
3 months of tumor removal were recorded. Residual
morbid states were assessed 3 months after the operation
and recorded as persistent morbid states.

**Statistical Analysis**

The results are shown as mean values ± standard devia-
tions. Several groups were compared using the chi-square
test, Welch test, Fisher exact test, or Mann–Whitney U-test.
All calculations were performed with the aid of Statview
statistical software (version 5.0; Abacus Concepts, Inc.,
Berkeley, CA).

**Results**

Between 1989 and 2003, 1434 cases of meningioma were
registered in the Kumamoto University Brain Tumor Data
Bank (Table 1). Of these, 603 (42.1%) were asymptomatic and
831 (57.9%) were symptomatic. Among the 603 pa-
tients without symptoms, 244 (40.5%) were 70 years of age
or older and 489 (81.1%) were female, whereas among the
831 patients with symptoms 229 (27.6%) were 70 years of age
or older and 569 (68.5%) were female. There were sig-
ificant differences (p < 0.001, chi-square test) with respect
to age and sex between patients with and without symp-
toms.

Of the 603 patients with asymptomatic meningioma, 351
(58.2%) were surgically removed. The criteria for surgery
included unusual increase in size.

Of the 603 initially asymptomatic meningiomas, 213
(35.3%) were surgically removed. The criteria for surgery
was recorded as persistent morbid states.

**TABLE 1**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Asymptomatic (%)</th>
<th>Symptomatic (%)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (yrs) (603 patients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70</td>
<td>359 (59.5)</td>
<td>602 (72.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥70</td>
<td>244 (40.5)</td>
<td>229 (27.6)</td>
<td></td>
</tr>
<tr>
<td>sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>114 (18.9)</td>
<td>262 (31.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>female</td>
<td>489 (81.1)</td>
<td>569 (68.5)</td>
<td></td>
</tr>
</tbody>
</table>

* Chi-square test.

**Surgically Treated Lesions**

Of the 603 initially asymptomatic meningiomas, 213
(35.3%) were surgically removed. The criteria for surgery
were dependent on the neurosurgeon’s determination in
each institute. No surgically treated patients died within 3
tumor size of 6 cm did not change throughout the course of
her 4.6-year follow-up; however, the minimum size of the
lesion increased from 4.5 to 6 cm. The mean initial tumor
size in this group of 10 patients was 3.7 cm (range 2.4–6
cm); it grew to 4.6 cm (range 3.5–6 cm) during a mean fol-
low-up period of 3.9 years. The tumors in this group of
patients were larger at the times of their initial and latest
measurement than those in patients who remained asym-
ptomatic or experienced no tumor growth. Regardless of
location, the mean diameter of the 383 asymptomatic me-
ningiomas at the time of diagnosis was smaller than that of
the 165 symptomatic tumors (2.4 ± 0.9 cm compared with
4.3 ± 1.3 cm; Fig. 1). These findings suggest that asym-
ptomatic meningiomas larger than 3 cm at the time of detec-
tion may eventually be accompanied by symptoms if they
increase in size.

**TABLE 2**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Tumor Growth Group (25 patients)</th>
<th>No Growth Group (42 patients)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean age in yrs (range)</td>
<td>63.0 (17–83)</td>
<td>65.8 (36–88)</td>
<td>0.482*</td>
</tr>
<tr>
<td>follow up in yrs (range)</td>
<td>7.8 (5.2–12.9)</td>
<td>7.4 (5.0–13.6)</td>
<td>0.536*</td>
</tr>
<tr>
<td>max diameter in cm (range)</td>
<td>2.4 (0.5–6.0)</td>
<td>2.3 (1.0–4.4)</td>
<td>0.737*</td>
</tr>
<tr>
<td>no. of lesions (%) w/ calcification</td>
<td>6 of 21 (28.6)</td>
<td>19 of 34 (55.9)</td>
<td>0.048‡</td>
</tr>
<tr>
<td>hypointensity on T2-weighted MRI</td>
<td>11 of 18 (61.1)</td>
<td>9 of 25 (36.0)</td>
<td>0.042†</td>
</tr>
<tr>
<td>perifocal edema</td>
<td>5 of 21 (23.8)</td>
<td>3 of 25 (12.0)</td>
<td>0.293‡</td>
</tr>
<tr>
<td>tumor location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>convexity</td>
<td>7 (26.9)</td>
<td>9 (34.6)</td>
<td>0.245†</td>
</tr>
<tr>
<td>parasagittal</td>
<td>4 (15.4)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>falk</td>
<td>5 (11.4)</td>
<td>9 (34.6)</td>
<td></td>
</tr>
<tr>
<td>cerebellopontine angle</td>
<td>2 (7.7)</td>
<td>3 (11.5)</td>
<td></td>
</tr>
<tr>
<td>sphenoid</td>
<td>1 (4.5)</td>
<td>5 (5.4)</td>
<td></td>
</tr>
<tr>
<td>others</td>
<td>7 (26.9)</td>
<td>16 (61.5)</td>
<td></td>
</tr>
</tbody>
</table>

* Welch test.
† Mann–Whitney U-test.
‡ Fisher exact test.
months of surgery. As shown in Table 4, the incidences of morbidity in surgically treated patients were 12 patients (5.6%) with persistent morbid conditions; nine patients (4.2%) with medical conditions; 20 patients (9.4%) with surgery-related conditions; and 33 patients (15.5%) with neurological conditions. Among the 54 patients 70 years of age or older at the time of surgery, 9.3% continued to manifest symptoms 3 months after the operation compared with 4.4% of patients younger than 70 years of age. As shown in Table 5, the persistent morbidity rate was lower in patients whose meningiomas were asymptomatic at the time of detection. However, this rate exceeded 6% in patients whose meningiomas were located in the convexity or falx, regardless of whether the tumors were symptomatic or asymptomatic. In patients harboring parasagittal or sphenoid ridge meningiomas, the morbidity rate was similar, irrespective of whether symptoms appeared. These results indicate that surgery for asymptomatic meningiomas is not necessarily safe.

In summary, we found that 63% of asymptomatic menin-
Indications for surgery for asymptomatic meningiomas

Table 4

<table>
<thead>
<tr>
<th>Type of Morbid Condition</th>
<th>Age &lt;70 Yrs (159 patients)</th>
<th>Age ≥70 Yrs (54 patients)</th>
<th>Total (213 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>medical</td>
<td>6 (3.8)</td>
<td>3 (5.6)</td>
<td>9 (4.2)</td>
</tr>
<tr>
<td>surgery related</td>
<td>16 (10.1)</td>
<td>4 (7.4)</td>
<td>20 (9.4)</td>
</tr>
<tr>
<td>neurological</td>
<td>27 (17.0)</td>
<td>6 (11.1)</td>
<td>33 (15.5)</td>
</tr>
<tr>
<td>persistent</td>
<td>7 (4.4)</td>
<td>5 (9.3)</td>
<td>12 (5.6)</td>
</tr>
</tbody>
</table>

* See Clinical Material and Methods for examples of the various types of morbid conditions.

Discussion

To develop an effective therapeutic strategy to treat asymptomatic meningiomas, investigators must gain a better understanding of their natural history, that is, incidences of tumor growth and symptomatic change. Furthermore, indications for surgery should be considered by comparing the surgical morbidity rates for asymptomatic and symptomatic meningiomas.

Incidence of Tumor Growth

In our study of the literature, the reported incidence of tumor growth during the follow-up period ranged from 0 to 37%.6,7,13–15 In the study reported by Firsching and associates,6 none of their 17 patients had an increase in tumor volume greater than 1 cm³ per year within the mean follow-up period of 1.3 years. On the other hand, Yoneoka and colleagues15 reported that 24.3% of observed meningiomas increased in maximum tumor size during a mean follow-up period of 4.2 years. One reason for these variations may be due to the difference in follow-up periods. Although many reports have provided data for follow-up periods of up to 3 years,6,11,13,14 recently Herscovici, et al.5 indicated that 19 (37%) of 51 meningiomas grew during a 6-year period. Their observation was very similar to ours, in which there was a 37.3% rate of tumor growth in 67 patients with asymptomatic lesions who participated in follow up for a mean of 7.8 years. According to the literature, at least two thirds of asymptomatic meningiomas do not continue to grow.

Speed of Tumor Growth

Olivero and colleagues14 found a tumor growth rate of 0.24 cm per year. Nakamura, et al.,11 who calculated tumor-doubling time in 41 patients, found a mean growth rate of 0.796 cm³ per year (range 0.03–2.62 cm³/yr), resulting in a 14.6% increase in volume per year and a mean tumor-doubling time of 21.6 years. Similar findings have been made in other studies.6,15 We found tumor growth in 25 (37.3%) of 67 asymptomatic meningiomas that were followed for longer than 5 years. In these lesions the growth rate, calculated using the maximum tumor diameter, was 1.9 mm/year, which is consistent with other rates found in previous studies. Although the average tumor growth rate cannot be compared directly among different studies because various measurement methods were used, most asymptomatic meningiomas exhibit minimal growth.

Factors Associated With Tumor Growth

Reported factors related to the growth of asymptomatic meningiomas include: advanced patient age,14,15 a hyperintense lesion on T₂-weighted MR images,10,13 and/or calcification.7,11,13 Consistent with the findings of other investigators, we observed a significant relationship between tumor growth and the finding of a hyperintense lesion on T₂-weighted MR images, and we found a higher incidence of tumor calcification in patients who did not experience tumor growth. Our search of the literature failed to uncover reports on the relationship between the histological characteristics of asymptomatic meningiomas and their growth rate. In our series, among 133 surgically removed asymptomatic meningiomas, histological investigations showed that six (4.5%) were atypical and two (1.5%) were malignant meningiomas.
Rate of Symptomatic Change

We observed that 11 (6.4%) of 171 patients with asymptomatic meningiomas later experienced symptoms; the rate was 20% among 25 patients whose asymptomatic meningiomas increased in size during the mean follow-up period of 7.8 years. In the literature, the rates at which initially asymptomatic tumors become symptomatic are listed as 3.1% in one study and 5.4% in another, rates consistent with that in our study. Only the report by Niirou, et al., showed a higher rate, 12.5% of 40 patients, but these authors restricted their study to patients older than 70 years. The critical size of a tumor that is associated with developing symptoms is not clear. Go and coworkers described a patient in whom seizures developed. In that case, the woman’s previously asymptomatic meningioma grew from 3 to 5 cm in maximum diameter over a 31-month period. In five of the patients described by Niirou, et al., the tumors grew from a mean of 3.9 cm (range 3–6 cm) to 6.3 cm (range 3.8–8.2 cm). In our series, 10 of 11 patients who began to experience symptoms presented with tumor growth. The initial size of the tumors these patients harbored (mean size 3.9 cm) was larger than that of patients who never experienced symptoms (mean size 2.3 cm). The mean tumor size at presentation with symptoms was 4.6 cm (range 3.5–6 cm), which is similar to sizes listed in reports in the literature. Interestingly, in our series, regardless of their location, the mean size of symptomatic tumors (4.3 ± 1.3 cm) was larger than that of asymptomatic meningiomas (2.4 ± 0.9 cm). From these data we infer that asymptomatic meningiomas that grow larger than 4 cm may be accompanied by symptoms. Conversely, even if a tumor exhibits growth, it may not develop symptoms as long as it remains smaller than 3 cm. In the literature, the rates of symptomatic change in asymptomatic meningiomas are 3 to 6%.

Surgery-Related Morbidity Rate

Although the usual treatment for meningioma is surgery, high rates of mortality and morbidity have been associated with surgical procedures, especially in elderly patients. Awad and colleagues reported a surgery-related mortality rate of 6.6% and a perioperative morbidity rate of 48% in 75 patients with meningiomas who were older than 60 years. Chan and Thompson found that, among 257 patients surgically treated for meningioma with a mean age of 53.1 years, the perioperative mortality and morbidity rates were 4 and 30%, respectively. These results indicate that meningioma surgery is not without risks, especially when performed in the elderly. We previously reported that, among 87 patients with asymptomatic meningiomas who were younger than 70 years, the perioperative morbidity rate was 3.5%; in the current series this rate increased to 4.4%. Although the average surgery-related morbidity rate was lower in patients with asymptomatic lesions than in those with symptomatic meningiomas, at more than 6% in cases in which asymptomatic tumors were located at the convexity or falx region this rate was comparable to that of the natural course of asymptomatic meningiomas. Also with respect to tumors located in the parasagittal or sphenoid ridge regions, the surgery-related rate of morbidity approached that noted in patients with symptomatic meningiomas. Furthermore, among our patients older than 70 years, the surgery-related morbidity rate was 9.1%.

Conclusions

Based on the results of this study and on those of previous studies, we suggest that surgery is not indicated in most patients with asymptomatic meningiomas and that these patients should instead be followed up closely by using neuroimaging and clinical monitoring. Tumors larger than 3 cm that are free of calcification and present as hyperintense regions on T2-weighted MR images, and tumors located in important anatomical structures in younger patients must be watched carefully. We recommend that, initially, these meningiomas should be reexamined after a 3-month interval to rule out the possibility that the lesion is malignant and again at 6-month intervals to detect tumor growth. If tumor growth is not detected, the lesion should be reexamined at 1-year intervals. We emphasize that radical surgery in elderly patients with asymptomatic meningiomas is not reasonable because the morbidity rate in this group of patients is higher than the rate of symptom development. In asymptomatic patients, close attention must be paid to the manifestation of even minor symptoms.

Acknowledgments

We are very grateful to Drs. J. Hamada, M. Morioka, and Y. Kai for their advice and discussions.

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Manuscript received August 1, 2005.
Accepted in final form March 1, 2006.
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