Natural history of elderly patients with asymptomatic meningiomas

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Abstracts

Objective—For the treatment of elderly patients with asymptomatic meningiomas, it is important to determine their natural history. Based on results of follow up examinations, the natural history of such patients was clarified and prognostic factors concerning the potential of tumour growth in the aged were identified.

Methods—The clinical records and imaging studies of 40 elderly (over 70 years) patients with asymptomatic meningiomas were analysed. The patients were followed up with repeated imaging studies, and changes in tumour size, clinical signs, and outcomes were evaluated.

Results—There were 32 women and eight men with a mean age of 76.1 years. The mean follow up period was 38.4 months, ranging from 6 to 97 months. Six patients died during the follow up period from disorders other than the tumours, and one patient died as a result of the tumour. Twenty six patients (mean follow up period 41.8 months, range 10–97 months) showed no tumour growth. Fourteen patients showed tumour growth (mean follow up period 32.1 months, range 6–88 months). Five (four men and one woman) of these patients became symptomatic. Based on imaging analysis (1) calcification of the tumour was associated with no tumour growth ($p=0.036$), and (2) the tumour size at the initial diagnosis was related to subsequent tumour growth ($p=0.016$). Other possible factors related to tumour growth included sex and hyperintensity on MRI T2 weighted images.

Conclusion—In elderly patients with asymptomatic meningiomas, careful clinical follow up with imaging studies is important. The imaging features mentioned may contribute to prediction of tumour growth.

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With the increase in the number of elderly people and advances in diagnostic imaging modalities, the frequency of detection of brain tumours in aged patients is increasing. It has been reported that the frequency of incidental detection of meningiomas is higher in aged patients than in non-aged patients.^{1–3} Because meningiomas are fundamentally benign

tumours that can be surgically removed, surgical treatment is recommended for patients with symptomatic meningiomas, even in aged patients. However, surgical removal in elderly patients is reported to be associated with significant morbidity and mortality.^{4–8} When considering the treatment for aged patients with asymptomatic meningiomas, it is important to know the natural clinical course of these patients. However, studies on the natural history of patients with meningiomas are rare.^{2,9–12} Furthermore, no such studies have examined aged patients. The purpose of this study was to clarify the natural history of elderly patients with asymptomatic meningiomas and to identify prognostic factors concerning the potential of tumour growth.

Patients and methods

A total of 92 aged (over 70 years) patients with meningiomas were investigated at the Department of Neurosurgery, Kagoshima University Hospital and its affiliated hospitals over the past 5 years. Among them, 69 were asymptomatic and 23 were symptomatic. We retrospectively analysed the clinical records and imaging studies of patients with asymptomatic meningiomas. Patients who were newly diagnosed during this time and patients with asymptomatic meningiomas who were still receiving follow up examination were included. The earliest patient included in this study had been first seen 6 years before the above mentioned study period. Among the patients with asymptomatic meningiomas, 16 patients who were not studied and 13 patients who were selected for surgery or radiosurgery at the time of the initial diagnosis were excluded. The other 40 patients, who had repeated imaging studies, were included. Meningioma was diagnosed by the presence of an extra-axial dural based mass that was uniformly and markedly enhanced by contrast agent. We analysed the clinical features of these patients at diagnosis, taking into account the following items: major complaint(s) or reasons for initial examination which led to meningioma detection, tumour location, and tumour size. Tumour size was defined as the maximum diameter on CT or MRI. Tumour growth was defined by the judgement of more than two persons among the coauthors. In judging the slight changes in tumour size, such as <5 mm, volumetric assessment by MRI was used to exclude inter-observer variability. The changes in tumour size, the clinical signs, and outcomes were evaluated.

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Table 1 Location of tumours and number of tumours at each location

Location of tumours	Number of tumours
Supratentorial	35
Convexity	9
Falx	8
Sphenoid ridge	5
Parasagittal	4
Tentorium	4
Frontal base	3
Tuberculum sellae	1
Cavernous sinus	1
Infratentorial	5
C-P angle	2
Cerebellar convexity	3
Total	40

C-P=cerebellopontine

We also examined the features of the asymptomatic meningiomas shown by imaging studies: the tumour size at the initial diagnosis, calcification of the tumour, accompanying brain oedema, and the signal intensity of the tumour on T2 weighted images. Calcification of the tumour included diffuse or partial calcification, but excluded small spotty calcification. Brain oedema was classified as being present or absent. Signal intensity of the tumour on T2 weighted images was compared with that of grey matter.

Statistical analysis was performed with the Statview software program (version 4.0, Abacus Concepts Inc, Berkeley, CA, USA). χ^2 test for independence or unpaired Student's *t* test was used appropriately to compare proportions. A *p* value < 0.05 was considered significant.

Results

The subjects consisted of 32 women and eight men with a mean age of 76.1 years (range 70 to 95 years). The diagnosis of asymptomatic meningiomas was made if the location and size of the tumour did not explain the patients' symptoms. Common symptoms in such patients were headache, dizziness, gait disturbance, and mental signs. Meningiomas were also incidentally detected during neuroradiological examination for other disorders of the CNS such as cerebrovascular disease, head trauma, screening for metastatic brain tumour, and parkinsonism.

Most tumours were located supratentorially (87.5%) and common tumour locations were convexity, falx-parasagittal area, sphenoid

ridge, and tentorium. Several tumours were located on the skull base (table 1). The average tumour size at the initial diagnosis was 26.0 mm in diameter (median 25 mm, range 10–60 mm). The mean follow up period was 38.4 months (median 36 months, range 6–97 months). Six patients died during the follow up period due to disorders other than tumours, and one patient died as a result of the tumour.

Twenty six patients (65%) showed no growth in their tumours. The average tumour size was 23.3 mm (median 22 mm, range 8–40 mm). The mean follow up period was 41.8 months (median 36 months, range 10–97 months). No treatment was given to patients with asymptomatic meningiomas that showed no tumour growth.

Fourteen patients (35 %) showed tumour growth (table 2). Five of them were men. The average tumour size was 30.9 mm (median 30 mm, range 18–60 mm). The mean follow up period was 32.1 months (median 30 months, range 10–88 months). Five (four men and one woman) of these 14 patients became symptomatic. The average tumour size of this subgroup was 39.0 mm at the initial diagnosis. Three of five patients with symptomatic meningiomas underwent surgery. The other two continued to be followed up because of old age and poor medical condition. One patient (case 13 in table 2) gradually developed right hemiparesis with mental symptoms, followed by disturbance of consciousness, and died 88 months after the initial diagnosis (figure). Six of nine patients with asymptomatic but growing meningiomas were treated by gamma knife radiosurgery.

The imaging findings of the asymptomatic meningiomas that were followed up by repeated imaging studies are summarised in table 3. The initial mean tumour size that showed tumour growth was 30.9 (SD 10.8) mm, significantly larger than that of the cases that showed no tumour growth (*p*=0.016). Nineteen tumours showed calcification and 16 of these did not show growth. Tumours with calcification grew significantly less than those without calcification (*p*=0.037). The mean size of tumours with calcification was smaller than that of those without calcification. Generally, asymptomatic tumours were not associated with brain oedema. Growing tumours were

Table 2 Follow up outcome and treatment of 14 aged patients with initially asymptomatic but growing meningiomas

No	Age and sex	Tumour location	Initial size (mm)	Final size (mm)	Follow up period (months)	Outcome and treatment
1	70/F	Lt clinoid	18	21	24	Asymptomatic, radiosurgery
2	72/F	Rt parietal falx	20	30	60	Asymptomatic, followed up
3	78/F	Lt cerebellar convexity	24	27	12	Asymptomatic, radiosurgery
4	71/F	Lt sphenoid ridge	25	30	38	Asymptomatic, followed up
5	74/F	Rt C-P angle	25	35	48	Asymptomatic, radiosurgery
6	79/F	Lt cerebellar convexity	28	31	6	Asymptomatic, radiosurgery, operation
7	74/M	Rt frontal convexity	30	65	6	Symptomatic, operation
8	72/M	Rt frontal falx	30	58	18	Symptomatic, operation
9	73/M	Rt frontal base	30	35	48	Asymptomatic, radiosurgery
10	76/F	Rt tentorium	30	34	24	Asymptomatic, followed up
11	73/F	Rt frontal falx	30	38	29	Symptomatic, operation
12	70/F	Rt cavernous	38	42	6	Asymptomatic, radiosurgery
13	74/M	Lt sphenoidal ridge	45	82	88	Symptomatic, died from tumour
14	85/M	Rt frontal convexity	60	72	36	Symptomatic, followed up

Average age was 74.5 years. The mean initial tumour size was 30.9 (18–60) mm in diameter.

The mean follow up period was 32.1 months (6–88 months).

C-P = cerebellopontine, Lt = left, Rt = right

T1 weighted images with contrast enhancement in 1991 (A) and in 1998 (B). (A) MRI showed the left sphenoidal ridge meningioma 45 mm in diameter at initial diagnosis. (B) MRI showed remarkable tumour growth with midbrain compression. The patient died 1 month later.

associated with brain oedema. However, brain oedema at the initial diagnosis showed no relation to tumour growth. Twenty seven patients underwent MRI; 14 with growing tumours, and 13 with non-growing tumours. Seven of 14 growing tumours showed hyperintensity on T2 weighted images. By contrast, only three non-growing tumours showed hyperintensity on T2 weighted images. Although a significant difference was not found, the meningiomas in aged men tended to grow.

Discussion

Among incidentally detected brain tumours, the most common benign primary brain tumour is meningioma,^{2 5 13} and incidental detection is more frequent in elderly persons than in young persons.^{1-3 13 14} With advances in surgical techniques and the medical management of aged patients, surgical treatment for symptomatic meningiomas may be indicated even for elderly patients.^{4-7 15 16} However, the resection of meningiomas in elderly patients is reported to be associated with significant morbidity and mortality.⁴⁻⁸ Therefore, the advisability of surgery should be carefully considered in asymptomatic patients. Many cases of

meningioma are detected during investigation for other CNS disorders such as cerebral infarction, parkinsonism, and dementia. In addition, other elderly patients may have a large tumour not associated with any focal neurological signs.

An important problem is the lack of information about the natural history of asymptomatic meningiomas. Asymptomatic meningiomas tend to be detected in elderly and female patients.^{1-3 17} Among symptomatic patients, a large proportion of unoperated aged patients died or their condition worsened from causes related to intracranial pathology within 1 to 5 years after the diagnosis.⁴ In aged asymptomatic subjects, the natural history has not been examined. It has been reported that most asymptomatic meningiomas, including those in young patients, remain asymptomatic and have a zero or slow growth rate after follow up periods varying from 21 months to 8.8 years.^{3 9-11} In a study of relatively aged subjects (mean age 67 years) with relatively long follow up periods (mean of 74 months), four of 35 tumours had become enlarged, and one patient developed symptoms related to the tumour.¹² Considering the clinical courses of the asymptomatic meningiomas in our study, two thirds of the patients with asymptomatic tumours did not show tumour growth for several years. On the other hand, one third of patients showed tumour growth, and about 10 % of patients who were initially asymptomatic became symptomatic. Most of the tumours that showed clear growth grew between 6 months to 2 years of diagnosis. In our study, the earliest observation period to confirm tumour growth was 2 months. This patient showed rapid tumour growth. The tumour was located in the right

Table 3 The imaging features of 40 asymptomatic meningiomas and the factors related to tumour growth

	Tumour growth (n=14)	No tumour growth (n=26)
Tumour size at initial diagnosis*	30.9 (10.9)	23.3 (8.1)
Calcification†	3/14	16/26
Brain oedema	2/14	7/26
Hyperintensity on MRI T ₂ weighted image	7/14	3/13
Sex (M:F)	5:9	4:22

Tumour growth v no tumour growth.
*p=0.016 unpaired Student *t* test.
†p=0.037 χ^2 test.

frontal convexity, grew to 65 mm in diameter 6 months after the initial diagnosis, and was removed surgically. The pathology of the surgical specimen indicated a transitional meningioma, but a high rate of positive MIB-1 stained cells was obtained.

The accuracy of measurement of tumours is a fundamental issue. Slight change in size on sequential imaging might possibly be due to slight differences in positioning of patients and timing of contrast administration. We attempted to get the same slice as that of the previous scan as much as possible. However, slight changes, such as those of several mm could not be regarded as definitive. By measurement on CT, most tumour growth was defined as an increase in diameter >5 mm. The slight changes, such as those <5 mm, were defined by MRI. In judging such slight changes, three dimensional measurement or volumetric assessment using MRI was helpful to exclude interobserver variability.

Some factors are considered to be associated with tumour growth. One characteristic finding of the imaging studies of our series was calcification of the tumour. Such tumours usually do not grow because of reduced proliferating potential, as verified by the MIB-1 staining index.¹⁸ One of the characteristic features of patients who showed tumour growth was the initial tumour size. In our study, moderate or large tumours (over 30 mm) showed a greater propensity to grow. Based on the clinicopathological MIB-1 staining index,¹⁸ a weak correlation was found between tumour size (>3.5 cm) and proliferative index. We should, therefore, recognise that a non-calcified meningioma with a moderate to large size has the potential to grow. Signal intensity on T2 weighted images has a fairly strong correlation with the histological subtype.¹⁹ Hypointensity reflects a fibrous and hard component.^{20, 21} A fibrous and hard tumour may show low proliferating potential.¹⁸ The meaning of hyperintensity is uncertain, but it might relate to proliferating potential. In our study, seven of 14 growing meningiomas showed hyperintensity or mixed hyperintensity on T2 weighted images. Considering the above mentioned imaging features, calcification, initial tumour size >30 mm, and signal intensity on T2 weighted images are thought to provide useful information to predict the growth potential of meningiomas. Asymptomatic meningiomas were four times more often detected in women than in men in our study. In growing tumours, the number of male patients tended to increase, compared to non-growing tumours. In particular, symptomatic patients were male dominant.

For the treatment of asymptomatic meningiomas, careful clinical follow up with repeated imaging studies is important. Because malig-

nant meningiomas may grow rapidly and these tumours cannot be definitively diagnosed by imaging studies alone, we recommend follow up study for 2 or 3 months after the initial diagnosis. If the absence of malignancy can be confirmed, 6 month or 1 year follow up intervals would be sufficient.

Conclusion

In elderly patients with asymptomatic meningiomas, because some tumours did grow and became symptomatic, careful clinical observation with repeated imaging studies is of primary importance. The imaging study findings mentioned above contribute to the prediction of tumour growth potential.

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