ORIGINAL

Histological characteristics of incidentally-found growing meningiomas

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Abstract : *Object*. With the wider use of CT and MRI, many meningiomas are discovered as incidental findings during diagnostic work-up for unrelated symptoms. The majority shows no or minimal growth. The purpose of this study was to distinguish pathological features of incidentally-found growing meningiomas by comparing incidentally-found with symptomatic meningiomas. *Methods*. One hundred and thirty two consecutive non-recurrent surgically-treated meningiomas treated between 2005 and 2007 were divided into three categories : 19 incidentally-found growing meningiomas (IG), 50 incidentally-found meningiomas (I), and 63 symptomatic (S) meningiomas. The average follow-up period for the IG meningiomas was 3.7 years. Six out of 19 patients of the IG meningiomas became symptomatic during observation. *Results*. There is a significant difference of the incidence of WHO grades I, II, and III between all three groups (p=0.035). The incidence of WHO grades II and III in groups IG, I, and S were 26%, 2%, and 10%, respectively. We compare MIB-1 staining index between three groups : an average was 3.8% in IG, 1.3% in I, and 2.4% in S meningiomas. *Conclusions*. Incidentally-found meningiomas need careful follow-up. One fourth of the meningiomas that showed signs of growing belonged to the atypical or malignant grade. J. Med. Invest. 59 : 241-245, August, 2012

Keywords : *growth, histological subtype, incidental, meningioma, MIB-1*

INTRODUCTION

Autopsy studies showed that an estimated 2-3% of the population has an incidental asymptomatic meningioma (1). With the wider use of CT and MRI, many meningiomas are discovered as incidental findings during work-up for unrelated symptoms (2). The majority of incidental menigiomas show no or minimal growth, therefore they can be safely observed with follow-up imaging until they grow significantly or become symptomatic (3-6). However, it is well known that some of them grow rapidly (4, 7, 8). Few authors have investigated pathological features of incidental meningiomas. The purpose of this study was to distinguish pathological features of incidentally-found growing meningiomas by comparing incidentally-found with symptomatic meningiomas.

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MATERIALS AND METHODS

One hundred and thirty-two consecutive patients with non-recurrent meningiomas were surgically treated in our Department of Neurosurgery between 2005 and 2007. The medical records of these patients were reviewed retrospectively.

The menigiomas were divided into three categories : incidentally-found growing meningiomas (IG), incidentally-found meningiomas(I), and symptomatic meningiomas (S). Incidentally-found meningiomas initially treated conservatively and finally removed surgically due to an increase in size were defined as IG. No meningiomas were previously treated by gamma knife radiosurgery. Incidentally-found menigiomas removed without a follow-up period were defined as I. Meningiomas surgically removed due to symptoms caused by the tumors were defined as S.

Radiological features were analyzed by CT scans and/or MRI. The position of the tumor was classified as follows : convexity, falx, parasagittal, sylvian fissure, tentorial, ventricular, foramen magnum, olfactory groove, petroclival, petrous, sphenoid ridge, and tuberculum sellae. The latter six positions were considered to be the skull base. The tumor volume was calculated using the formula : length × depth × width × 0.5 (2) on the enhanced MRI. Based on conventional CT and bone window CT, patients were divided into two groups according to the low density area around the tumor and calcification in the tumor.

The tumors were histologically classified according to the World Health Organization classification of tumors (9). An avidin-biotin immunoperoxidase or simple stain MAX-peroxidase (Nichirei, Tokyo) technique was used to perform MIB-1 monoclonal antibody (DAKO, Denmark) assay in selected sections of each case (10). All tissue sections were examined at high-power magnification (× 400). The number of cells stained positively with MIB-1 and the total number of tumor cells were counted in several representative fields containing more than 1000 cells. Their ratio was indicated as the MIB-1 staining index (%).

STATISTICAL ANALYSIS

All data were stored on a personal computer and analyzed using commercially available statistical software (SPSS version 12.0, SPSS Inc.). Chi-square analysis was used to compare characteristics and histological grades of patients with meningioma between all three groups. The student t-test was applied to compare the MIB-1 staining index between two groups of three. Significance was judged at a value of $p < 0.05$ for all analyses.

RESULTS

Table 1 shows the characteristics of 19 incidentally-found growing, 50 incidentally-found, and 63 symptomatic meningiomas. Six out of 19 patients of incidentally-found growing meningioma became symptomatic during observation. Three suffered from convulsions, two patients developed cranial nerve palsy and one developed an exophthalmus. The average initial and final maximum diameters of these tumors in an axial plane were 17.6 and 24.6 mm during an average follow-up period of 3.7 years. The average maximum diameter increase of was 3.7 mm per year. Fifty-one patients with meningioma were over 60 years of age ; 33 patients were male ; 69 were symptomatic ; 65 meningiomas were located at the skull base ; 31 were more than 20 cm^3 in volume ; 43 had an accompanying edema ; 39 meningiomas showed signs of calcification. The difference in incidence at the skull base and the tumor volume were statistically significant between the groups (IG, I, S).

Table 1 Characteristics of the incidentally-found growing (IG), incidentally-found (I), and symptomatic (S) meningiomas

		Group		
Factor		IG	I	S
Age (years)	-49	2	15	23
	50-	9	14	18
	60-	3	18	11
	70-	5	3	11
Sex	male/female	6/13	8/24	19/44
Symptomatic	yes/no	6/13	0/50	63/0
Skull base*	yes/no	7/12	19/31	39/24
Volume*	-9.9	15	27	18
	10-	2	14	17
	20-	2	7	24
Edema	yes/no	5/14	13/37	25/38
Calcification	yes/no	6/13	18/32	15/48
Tatal		19	50	63

*$p < 0.05$

Table 2 shows the histological subtypes of the 132 surgically-treated meningiomas. There is a significant difference of the incidence of WHO grades I, II, and III between all three groups ($p=0.035$). The number of WHO grade II and III were 4 and 1 in 19 IG meningiomas ; one and zero in 50 I meningiomas ; and 4 and 2 in 63 S meningiomas. The incidence of grades II and III meningiomas in IG,

Table 2 Histological subtypes of the incidentally-found growing (IG), incidentally-found (I), and symptomatic (S) meningiomas.

	Group		
Subtype	IG	I	S
Grade I	14	49	57
Meningothelial	6	18	31
Fibrous	4	19	7
Transitional	4	7	15
Psammomatous	0	0	0
Angiomatous	0	4	1
Microcystic	0	0	0
Secretory	0	1	1
Lymphoplasmacyte-rich	0	0	1
Metaplastic	0	0	1
Grade II	4	1	4
Atypical	3	1	4
Chordoid	1	0	0
Grade III	1	0	2
Rhabdoid	0	0	0
Papillary	0	0	0
Anaplastic	1	0	2
Total	19	50	63

There is a significant difference of the incidence of WHO grades I, II, and III between the three groups (p=0.035).

I, and S group were 26%, 2%, and 10%, respectively. We compared the MIB-1 staining index between all three groups : the average was 3.8% in IG, 1.3% in I, and 2.4% in S meningiomas (Figure 1). There were statistically significant differences of MIB-1 staining index between IG and I, I and S, but not between IG and S. Two incidentally-found growing meningiomas are shown in Figure 2.

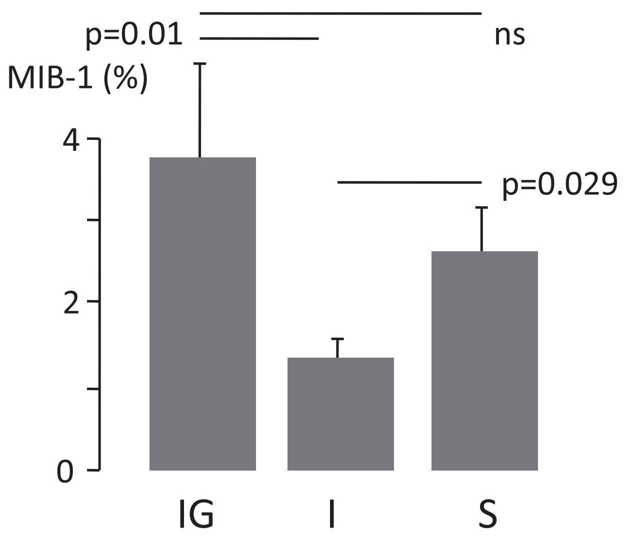

Fig. 1 Comparison of the MIB-1 staining index (mean±standard deviation) between incidentally-found growing (IG), incidentally-found (I), and symptomatic (S) meningiomas. There are statistically significant differences of MIB -1 staining index between IG and I, and I and S, but not IG and S.

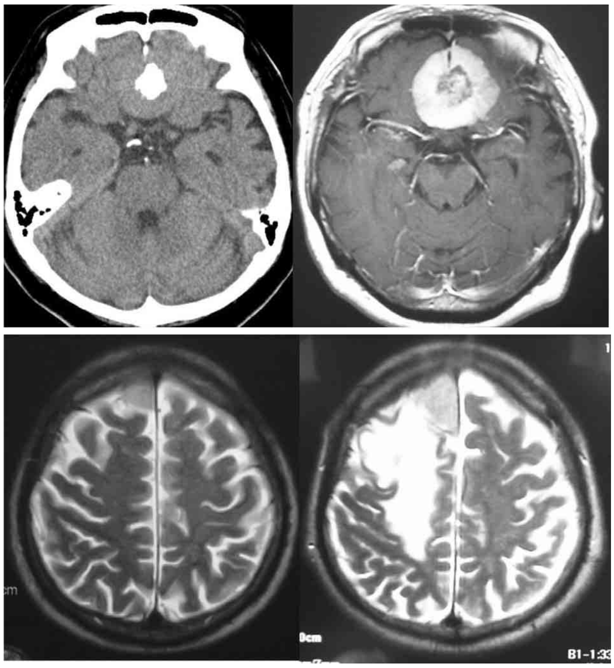

Fig. 2 An anterior skull base meningioma with calcification was incidentally found in an 83 year-old woman 8 years ago (upper left panel). She underwent surgery because of the increase in size (upper right panel) and subsequently the tumor was diagnosed as meningothelial meningioma with a MIB-1 index of 3.2%. A small right-sided parasagittal meningioma was detected during a routine check-up in February of 2003 (lower left panel). The size of the tumor increased significantly developing perifocal edema during a course of 3 years (lower right panel). The tumor was diagnosed as an atypical meningioma (MIB-1 index=11.6%).

DISCUSSION

In our study we were able to show that the incidence of WHO grades II and III meningiomas in IG was 26%, much higher than that of the I and S groups. The average MIB-1 staining index in IG was 3.8%, also higher than that found in the I and S groups. It would have been ideal if we could have compared the pathological characteristics between growing and non-growing incidental meningiomas. Retrospectively, we divided surgically-treated meningiomas into three categories and compared the pathological features. Meaning that incidentally-found (I) meningiomas removed without a follow-up period may include those of a growing type. However, the difference of pathological feature between IG and I meningiomas was clear. These findings indicate that meningiomas that have evidence of growing may be different from those without, may be biologically active and include more malignant characteristics.

The natural history of menigiomas has been studied extensively (4-6, 8, 9, 11-15). The follow-up of a total of 381 patients with menigioma for an average of 59 months revealed that the growing rate was between 17.5-37%, and the rate of change to becoming symptomatic was between 0-17.5%. We now know that the majority of menigiomas show no or minimal growth, and can be observed without any surgical intervention.

Few authors have investigated the relation between the natural history and the pathological features of meningiomas. Jaaskelainen *et al.* (7) estimated the mean size doubling time of recurrent meningiomas in 43 patients and found ranges from 450 days for benign, to 205 days for anaplastic tumors, to 178 days for atypical meningiomas. These results can not be applied to the course of the natural history of all meningiomas, including non-recurrent, as changes in histological morphology and malignant transformation are known to take place especially in recurrent meningiomas (2). Therefore, we highly recommend surgical removal or radiotherapy for recurrent meningiomasin timely manner.

Recently, Hashiba *et al.* (16) performed serial volumetric assessments throughout the follow-up period for longer than 1 year in 70 patients with incidentally discovered meningiomas and investigated the growth patterns of these lesions by regression analysis. Forty-four tumors exhibited growth and 26 did not. In a regression analysis, 16 of the tumors that grew followed an exponential growth pattern and 15 exhibited linear growth patterns. Two patients with meningioma of an exponential growth pattern underwent surgical removal. They consisted of an atypical and a meningothelial meningioma with a relatively high MIB-1 staining index : 5.8% and 9.0%. These results are similar to our experience.

Various predictive factors for tumor growth such as age, sex, tumor volume, and calcification, MRI T2 were reported. We analyzed the relationship of the MIB-1 staining indices to the characteristics of 342 consecutive patients with meningioma surgically removed between 1995 and 2004 (2). Logistic regression analysis demonstrated that male, recurrence, non skull-base, absence of calcification were independent risk factors for a high MIB-1 staining index ($\geq$3.0) ; age, symptomatic, volume, multiplicity, and edema were not. These results indicate that the growth rate of symptomatic meningiomas may almost be the same as that of incidental meningiomas.

In conclusion, incidentally-found meningiomas need a careful follow-up. One fourth of the meningiomas are of atypical or malignant grade once they have shown signs of growing. Attention should be paid to this fact because the management of these meningiomas is completely different from the benign types (17).

DISCLOSURE

There is no COI status to disclose. Hidetoshi Kasuya

There is no COI status to disclose. Osami Kubo

There is no COI status to disclose. Koichi Kato

There is no COI status to disclose. Boris Krischek

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