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Evaluation of Contributive Factors on Recurrence of Intracranial Meningioma

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Abstract

Background: Meningiomas are common benign tumors of the central nervous system. Patients with meningiomas achieve postoperative optimal functional recovery, but there is a probability of tumor recurrence months or years after surgical resection. This study aims to evaluate the prevalence of recurrent meningioma and the correlation between tumor recurrence and certain factors.

Materials and Methods: We performed a retrospective descriptive-analytical study of patients with meningiomas who underwent surgical treatment in hospitals affiliated with Shiraz University of Medical Sciences during a 20-year period (1988 to 2008). Factors including sex, age, bone changes, peritumoral edema, histological subtypes, tumor size, shape, location and resection degree, and recurrence time were evaluated in each patient.

Results: The recurrence rate of intracranial meningioma in a total of 644 patients included in the study was 10%. Statistical analysis of data showed a correlation between edema, bone changes, tumor size and shape, and histological subtypes. No relationship was found between age, sex and tumor location. This study has shown a statistical correlation between radiotherapy and a reduced probability of tumor recurrence or growth after surgical resection.

Conclusion: Although the majority of meningiomas are benign, they can have malignant presentations. Recurrence occurs after a shorter period of time in patients with malignant and atypical meningiomas than in patients with benign meningiomas. Edema, bone changes, large size, special tumor shape and malignant histological subtypes are important prognostic factors that predict the probability of tumor recurrence or growth. Findings show a statistical correlation between the degree of tumor resection and its recurrence. This study recommends a more complete tumor resection along with adjuvant therapy and closer follow-up to decrease the risk of tumor recurrence.

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Keywords: Recurrence, Meningioma, Intracranial tumors, Radiotherapy

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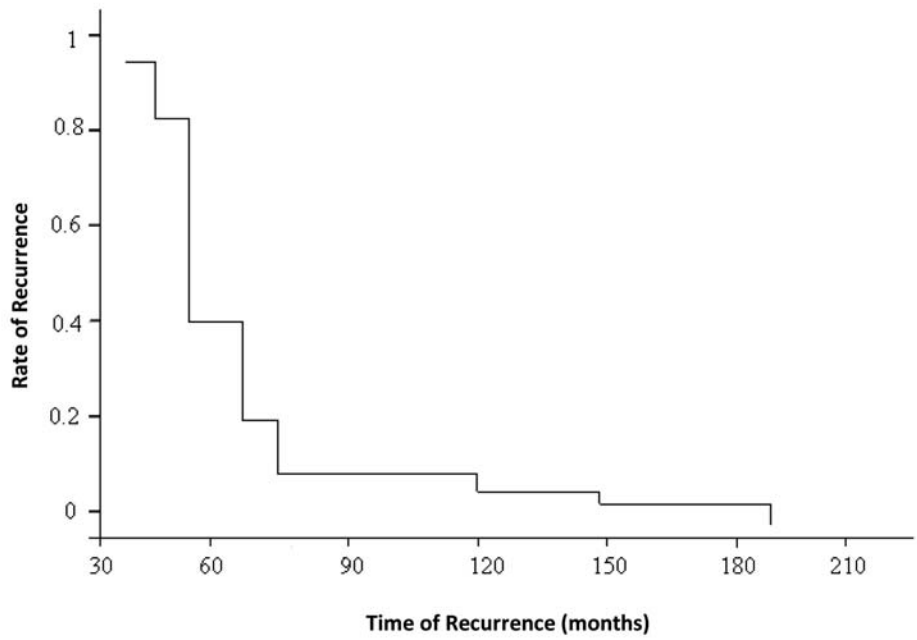

Figure 1. Follow-up curve in Kaplan-Meier showing the interval between surgery and recurrence.

Introduction

Despite technological advances in diagnostic devices, as well as new advancements in microsurgical techniques in neurosurgery and adjuvant therapies, the numbers of patients with recurrent intracranial tumors are increasing daily. Meningiomas are one of the most common benign tumors of the brain[1,2] that can cause different symptoms such as visual impairments, seizures, headaches, weakness and intracranial neurological disorders based on location. In recent decades, diagnosis and treatment of these tumors have remarkably improved. Complete tumor resection is a definite cure. Some patients should receive adjuvant therapy, such as radiotherapy, in addition to surgical removal of the tumor. However, occasionally the tumor can recur months or even years after surgical resection.[2-6] Because meningiomas occur mostly during the fourth and fifth decades of life and this age range includes an active population of the society; therefore a correct diagnosis, knowing the contributive factors on recurrence and receiving timely treatment can improve health levels and reduce mortality rates.[7] This study aims to evaluate the recurrence rate of intracranial meningiomas and correlation between certain factors and increased risk of tumor recurrence.

Materials and Methods

We performed a retrospective descriptive-analytical study in which 644 patients with meningiomas who underwent surgical treatment in hospitals affiliated with Shiraz University of Medical Sciences during a 20-year period (1988 to 2008) were included. All patients were studied in the out-patient clinic. A total of 10 patients missed their follow-up visits. Therefore, 634 patients were followed for a mean period of 13 years (6-20 years) and median of 10 years. A complete set of data including sex, age, bone changes, peritumoral edema, histological subtypes, tumor size, shape, location and resection degree, and recurrence time were evaluated in each patient by CT and MRI at six months following surgery and annually thereafter. Tumors were divided into two groups: the first group according to size (small: volume less than 30 ml, and large: volume greater than 30 ml) and the second group according to shape which included round, lobulated and mushroom. Tumor locations were divided into five groups as shown in Table 1. Skull bone was evaluated for the presence of hyperosteotic or osteolytic changes. Peritumoral edema was also evaluated. Tumor histology subtypes were classified into three groups that

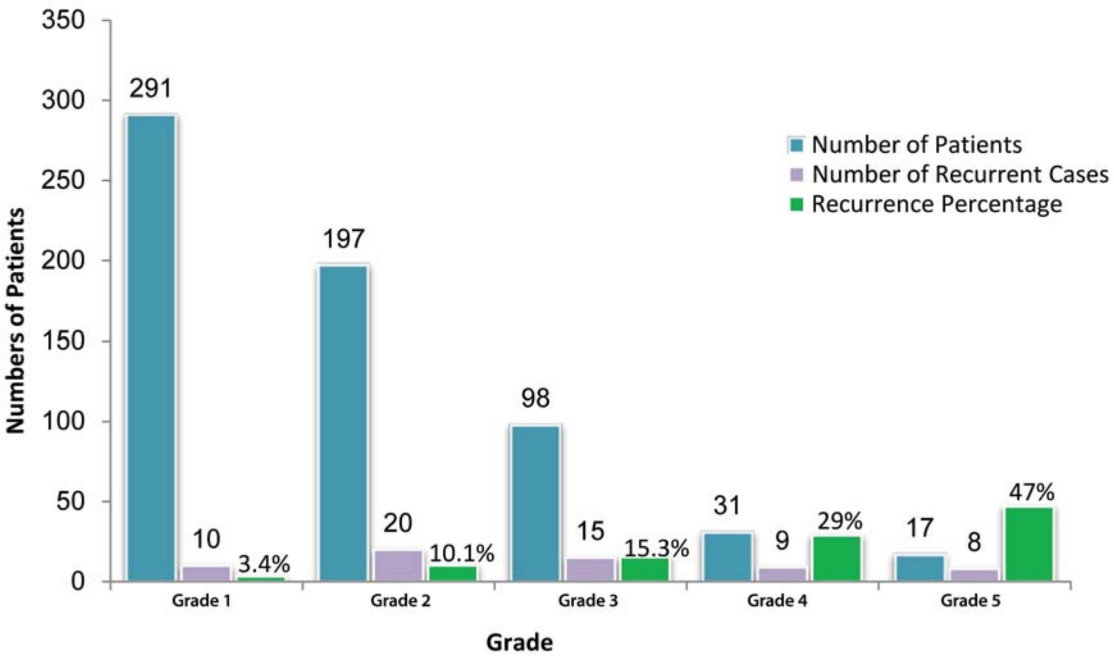

Figure 2. Recurrence rate according to the degree of surgical tumor removal (Simpson grade).

included classic (benign), anaplastic and malignant according to the Russell and Rubinstein classification. Malignant meningiomas were atypical and anaplastic. The degree of tumor resection was also estimated by Simpson criteria.

These data were studied in all meningioma cases until tumor recurrence or the end of this study. In addition, the interval between tumor resection and its recurrence was described by the Kaplan-Meier method (Figure 1).

For comparison of factors, Chi square or, when appropriate, Fisher's exact test were used. The data were statistically analyzed by SPSS for Windows 14 (SPSS Inc. Chicago, IL) software. Level of significance was statistically considered $P<0.05$.

Results

Out of 634 meningioma study patients, 63 (10%) developed recurrence during the mean observation period of 13 years (6-20 years). Of 215 male patients, there were 28 cases of recurrence (12.4%) and out of 419 female patients, 34 recurrence cases (8.1%) were seen ($P=0.76$). The distributions of patients and degrees of tumor recurrence among the different age groups are shown in Table 2. The highest rates of recurrence were 16.2% and 13% in age groups 2 and 3, respectively. The lowest recurrence rate was 4.6% in age group 6 ($P=0.15$).The correlation between age and recurrence was not statistically significant. Of 372 small size tumors, there were 28 cases that recurred (7.5%) and in 262 large size tumors, 34 recurrence cases (13%) were found, which were statistically significant ($P=0.014$). Among all patients, there were 301 cases of round tumors, 298 lobulated tumors and 35 mushroom tumors. In patients with round, lobulated or mushroom tumors a total of 24 (7.9%), 12 (4.1%) and 26 (74.3%) recurred, respectively. The mushroom tumor which had the most recurrence was statistically significant ($P=0.01$). Resulting data from the primary tumor location and the probability of tumor recurrence in each area are shown in Table 2. The highest recurrence was seen in the parasagittal and falx areas with 18 cases (11.8%). However, no statistical correlation was found between primary tumor location and the probability of its recurrence ($P<0.63$). Of the 634 patients, 459 had no peritumoral skull bone changes, however 140 and 35 patients had hyperosteotic and osteolytic changes, respectively. Of the groups with no bone changes, or hyperosteotic and osteolytic changes there were 47 (10.2%), 13 (9.3%) and 3 (8.6%) recurrent cases, respectively. A statistically significant

Table 1. Rate of recurrent intracranial meningioma according to tumor location.

Tumor location	Number of meningiomas	Number of recurrences	Recurrence percentage
First segment (parasagittal, falx)	152	18	11.8
Second segment (convexity)	195	20	10.3
Third segment (suprasellar/CP angle, tentorial, foramen magnum)	137	12	8.8
Fourth segment (sphenoid)	122	12	9.8
Fifth segment (olfactory groove)	28	1	3.6
Total	634	63	9.9

correlation was found between all types of bone change and recurrence ($P<0.05$). Of the 486 patients with peritumoral edema and 158 without peritumoral edema, there were 54 (11.1%) and 8 (5.1%) cases, in which tumor recurred that showed a significant correlation between edema and the probability of recurrence ($P=0.02$). Pathologically, 44 (7.4%) and 18 (38.3%) recurrent cases were found in 597 patients with benign tumors and 47 patients with atypical and malignant tumors, respectively. This showed a statistically significant correlation between malignant histology subtypes and the probability of tumor recurrence ($P<0.02$). Recurrence rate based on the degree of surgical tumor resection was estimated by Simpson criteria and shown in Figure 2. The highest recurrence rate was seen in grade 5 and the lowest was found in grade 1. Consequently, along with a rise in the number of grades, the probability of recurrence increased. There was a significant statistical correlation between the degree of tumor resection and recurrence ($P<0.01$). In the benign tumor group, the time interval until recurrence ranged from 10 until 170 months (14 years), with an average of 36 months. In the group with malignant tumors, recurrence ranged from 6 months until 68 months, with an average of 19 months. There was a significant statistical correlation between histology subtypes and the interval until recurrence ($P=0.001$). Thus, malignant tumors recur sooner. Findings have shown a significant reduction in meningioma recurrence 12 years after tumor resection, according to Kaplan-Meier analysis (Figure 1). Six patients (8%) in the malignant group, despite adjuvant radiotherapy, recurred three times. Five out of the total of 20 patients (25%) had tumors in the parasagittal sinus area, sphenoid and with extension into the ethmoid sinus who received radiotherapy after surgery that experienced recurrence. No statistically significant correlation was found between postoperative radiotherapy and recurrence ($P=0.15$).

Discussion

Meningiomas are common tumors comprising 19% of intracranial tumors and 25% of all tumors of the central nervous system.[4,5] In spite of the fact that these tumors are known as benign tumors, their recurrence is a noticeable point that requires further evaluation. Different studies have evaluated tumor recurrence and its contributive factors in order to lessen the probability of recurrence by introducing those groups of patients which are more at risk.[8-11] The recurrence rate is reported as 10.5% to 32% in various studies.[4,7] Studies performed by Mirimanal et al.[12,13], Mentel et al.[12,13], Yamasaki et al.6 and Adegbite et al.4 have verified the lack of statistical correlation between age, sex and the probability of recurrence. In this study, mushroom shape tumors have raised the probability of tumor recurrence whereas the least recurrence was seen among lobulated tumors. This was also confirmed in a study by Nakasu et al.[14] However, in another study by Yamasaki et al.[6], this relation was not found. In different studies, the degree of surgical tumor resection is the main contributive factor predicting recurrence rate with a strong statistical correlation. Thus, more surgical resection causes a decrease in the probability of recurrence. In the Yamasaki study, the recurrence rate was 9%, 16% and 29% in

Table 2. Rate of recurrent intracranial meningioma according to age.

Group	Age	Number of meningiomas	Number of recurrences	Recurrence percentage
1	≤20	21	2	9.5
2	21-30	65	11	16.9
3	31-40	120	17	14.2
4	41-50	150	16	10.6
5	51-60	169	12	7.1
6	61-70	91	4	4.4
7	≤ 71	18	1	5.5
Total	……..	634	63	9.9

tumor grades 1, 2 and 3, respectively. Mathiusem et al. have also described the recurrence rate in different degrees of resection. Tumor histology subtypes can be effective prognostic predictors of recurrence risk. In this study, it was determined that malignant tumors were more likely to recur at a shorter interval between tumor resection and recurrence. Additionally, atypical and malignant changes in a study performed in 1997[15], the presence of peritumoral edema in a Mantel study13 and bone changes in a Nakasu study have been introduced as contributive factors that increase the probability of recurrence[16,17], but the relation was not verified in the study by Yamasaki et al.[6]

In a study, most recurrences occurred during the first 10 years after tumor resection and were rare after 25 years.[16] This study has suggested a follow-up period of more than 10 years for all meningioma patients. The role of conventional or stereotactic radiotherapy in the management of some meningiomas is remarkable and we can use this technique as the only treatment or adjuvant therapy.[17-24] In most anaplastic tumor cases, total removal is impossible because of its anatomic location or when there is concern for potential damage to normal neurologic structures. In this study, radiotherapy was effective in recurrent meningiomas and in cases where total tumor removal was impossible.

Factors such as edema, bone changes, as well as tumors with a special shape, large size and malignant histology subtypes can predict tumor recurrence. A significant correlation was found between the degree of tumor resection and the probability of recurrence which showed that a more complete tumor resection decreased the probability of recurrence. This study has strongly suggested that the addition of post-operative radiation in cases of incomplete resections or malignant tumors prevents tumor recurrence and improves overall survival.

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