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Intracranial Meningiomas: Analysis of Recurrence After Surgical Treatment

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Summary

Recurrence of intracranial meningiomas after surgery has long been recognized, but there is still no consensus about factors responsible for recurrence. To better understand such factors, we analysed data on 276 patients with meningiomas who were treated at our institution from 1976 to 1990 (mean follow-up = 5.1 years). Effects of sex, tumour histology, tumour site, and radiotherapy on recurrence were closely studied. Using World Health Organization criteria to define malignancy, 254 of the tumours were benign and 22 were atypical or malignant. For data analysis, distinction was made between "recurrence" (i.e., reappearance of tumour after total resection) and "regrowth" (i.e., tumour enlargement after subtotal removal). Recurrence was seen in 2 of 183 benign meningiomas and in 10 of 16 malignant meningiomas. Recurrence and regrowth rates for malignant meningiomas far exceeded those for benign meningiomas ($p = 0.001$). Neither sex nor tumour site was associated with subsequent recurrences in patients whose tumours had been completely resected.

The influence of radiotherapy was studied in terms of its effects on benign versus malignant meningiomas, whether given after complete or incomplete resection, and whether given after primary resection or on reoperation. We found that radiotherapy did not decrease "recurrence" or "regrowth" regardless of when administered, either at first resection or on recurrence. This was true for benign as well as malignant meningiomas. However, due to the small number in our series, we cannot conclude that radiotherapy has no beneficial role in the treatment of meningiomas.

We do believe that the rate of recurrence for benign meningiomas is far lower than has been reported and that the majority of "recurrences" are in fact "regrowths" representing continuous tumour growth after incomplete removal. In fact, whenever recurrence is seen after complete surgical removal, chances are that tumour was atypical or malignant.

Keywords: Meningioma; recurrence; regrowth; radiotherapy.

Introduction

Meningiomas have been recognized as an entity for nearly two centuries[17]. Although generally considered benign, their behaviour is unpredictable and characterized by frequent recurrences. While a large proportion of these tumour recurrences can be attributed to incomplete primary excision, recurrence rates after complete excision have ranged from 9%[16] to 32%[13]. We believe the problem of recurrence in meningiomas remains unsolved because of a lack of consensus on both the definition of malignancy and the biological significance attached to histologic appearance. Also, most of the relevant literature predates the use of computed tomography and operative microscopy, which makes it difficult in those cases to assess the extent of resection as well as to recognize recurrence accurately.

We analysed our 15-year experience with meningiomas in an attempt to further elucidate those factors responsible for recurrence.

Patients and Methods

We reviewed medical records of 319 patients with intracranial meningiomas who were treated at Henry Ford Hospital between 1976 and 1990. Of these, 276 patients were included in the study. Forty-three patients were excluded because of multiple meningiomas, incomplete medical records, or a lack of pertinent surgical information on primary resection which in those cases had been performed at another hospital.

Surgical excision was graded according to Simpson's classification[16]; tumours known to have undergone Simpson's grade 1 or 2 surgical removal were designated as total resections and grades 3 to 5 as subtotal resections. Primary resection was total in 199 tumours and subtotal in 77. Eleven patients received radiation therapy after primary resection, because of either incomplete tumour removal or histologic evidence of malignancy. Ten patients received radiotherapy at tumour recurrence. To study the effect of radiotherapy on recurrent meningiomas, we compared subsequent progression of such tumours with that of recurrent cases that had undergone surgical resection without radiation therapy.

Histologic diagnosis of benign versus atypical and malignant meningiomas was based on six criteria outlined by the World Health Organization[10, 21]: hypercellularity, loss of architecture, nuclear pleomorphism, mitotic index, tumour necrosis, and brain invasion.

Follow-up data were obtained from hospital notes and radiographic studies as well as by contacting patients and their families. Mean follow-up was 5.17 years (62 ± 4 months).

Kaplan-Meier estimates were used to study recurrence rates in different groups. Log rank statistics were used to compare different groups.

Results

Of the 276 cases, 254 (92%) were benign and 22 (8%) atypical or malignant. The peak incidence occurred in the ninth decade (age range 11–84 years; mean 56 years). We noted a female preponderance in our series with a male to female ratio of 1 : 2.1. However, when separating benign and malignant cases, the male to female ratio was 1 : 2.3 for benign meningiomas and 1 : 0.9 for malignant meningiomas. Thus, malignant meningiomas lacked a female predominance. The most common tumour site was the convexity followed by parasagittal areas.

For data analysis, we defined "recurrence" as reappearance of tumour after total resection and "regrowth" as tumour enlargement after subtotal removal. We believe this distinction is important because recurrence and regrowth represent two separate phenomena. The diagnosis of recurrence was based on computed tomography or magnetic resonance imaging findings.

Overall, the mean time to tumour recurrence was 46 months. Recurrence rates for 1, 5, and 10 years were 1%, 7%, and 11%, respectively. However, of 199 completely resected tumours, the majority were benign (183 benign versus 16 malignant). Recurrence was seen in 2 benign and 10 malignant meningiomas. For benign meningiomas completely resected, mean recurrence time was 38 months. Recurrence rates for 1, 5, and 10 years were 0%, 2%, and 2%, respectively (Fig. 1). For malignant meningiomas completely resected, mean recurrence time was 48 months with 1-, 5-, and 10-year recurrence rates at 13%, 50%, and 75%, respectively

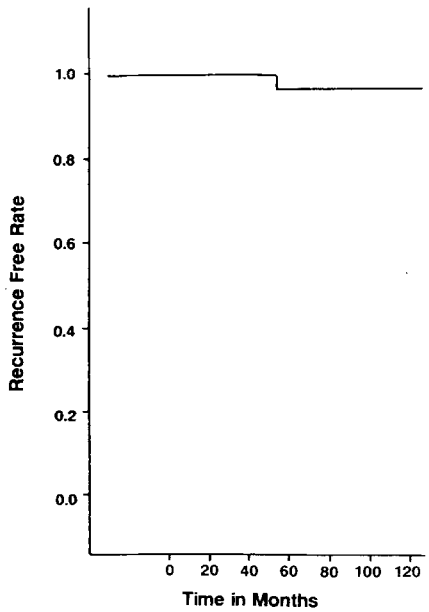

Fig. 1. Cumulative proportion of all patients with benign meningiomas free of recurrence after having undergone total resection

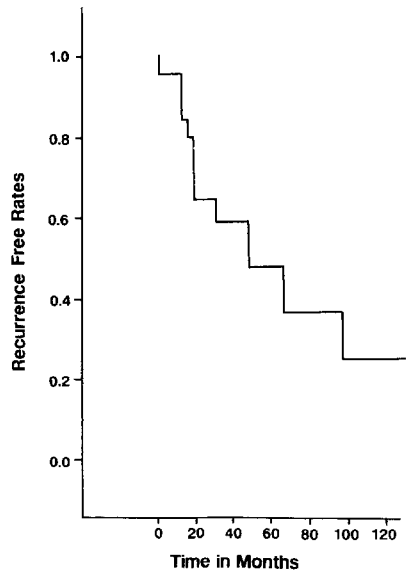

Fig. 2. Cumulative proportion of all patients with malignant meningiomas free of recurrence after having undergone total resection

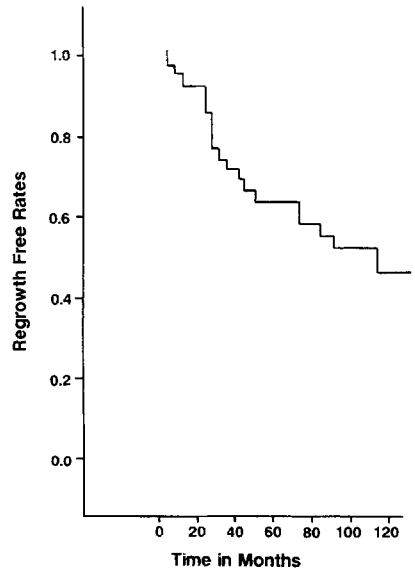

Fig. 3. Cumulative proportion of all patients with benign meningiomas free of regrowth after having undergone subtotal removal

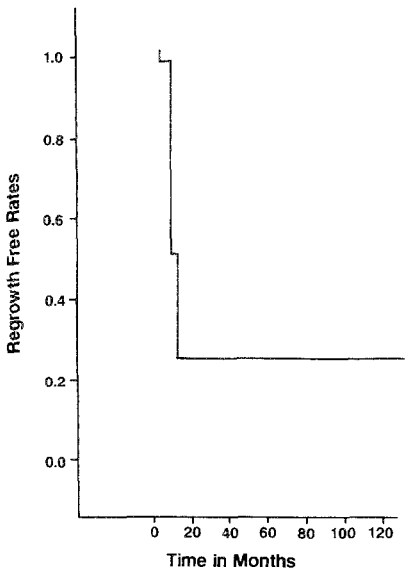

Fig. 4. Cumulative proportion of all patients with malignant meningiomas free of regrowth after having undergone subtotal removal

(Fig. 2). The difference between the two groups was highly significant ($p = 0.001$).

Among the subtotally removed tumours, 71 were benign and 6 malignant. Regrowth occurred in 29 benign and 4 malignant cases. The 1-, 5-, and 10-year regrowth rates for benign meningiomas were 18%, 46%, and 64%, respectively (Fig. 3), whereas the 1-year regrowth rate for malignant cases was 75% (all regrowth in malignant cases occurred in less than 5 years) (Fig. 4). Mean regrowth time for benign and nonbenign cases was 60.8 and 10.8 months, respectively. The difference between the two groups was statistically significant ($p = 0.001$).

We also evaluated the effects of sex, tumour site, and radiotherapy on tumour recurrence. Sex and tumour site were evaluated only for the totally resected cases. Recurrence was seen in 9 (14%) of 64 males and in 3 (2%) of 135 females ($p = 0.001$). However, this finding was significant primarily because malignant meningiomas were more frequent in males. When analysing benign and malignant meningiomas separately, sex had no bearing on tumour recurrence.

Recurrence was seen among 7% of tumours located at the convexity, 8% at parasagittal areas, and 15% at the olfactory groove (Table 1). This difference among sites regarding the potential to recur was not statistically significant and there was still no association when the analysis was performed separately for benign and malignant meningiomas.

Because benign and malignant meningiomas have different biological behavior, we studied the effects of radiotherapy separately in both groups.

Effects of radiotherapy on malignant meningiomas: Three malignant meningiomas were irradiated after primary resection (2 total resections and 1 subtotal removal). Recurrence was seen in the 2 totally resected tumours after an average of 12 months. In comparison, recurrence was seen in 8 of 14 cases in the nonirradiated, completely resected tumour group (mean recurrence time = 57 months; 1-, 5-, and 10-year recurrence rates = 14%, 43%, and 73%, respectively) (Table 2). The difference between the two groups was not significant ($p = 0.50$).

For malignant meningiomas subtotally removed, regrowth was seen in the 1 irradiated tumour and in 3 of 5 nonirradiated tumours. Mean recurrence time for the irradiated and nonirradiated meningiomas was 14 and 10 months, respectively. It was not possible to calculate 5- or 10-year regrowth rates because all regrowth occurred in less than 5 years (Table 3). Again, there was no statistical difference between the two groups ($p = 1.00$).

Table 1. *Recurrence Rate of Tumours at Different Locations*

Site	No. of patients with no recurrence	No. of patients with recurrence	Percent with recurrence
Convexity	71	5	7%
Parasagittal	33	3	8%
Olfactory groove	11	0	0%
Sphenoid ridge	23	4	15%
Intraventricular	5	0	0%
Tub sella	12	0	0%
Tentorium	9	0	0%
CPA	12	0	0%
Torcula	2	0	0%

Table 2. *Malignant Meningiomas.* Effects of radiotherapy after total resection

	Total number	No. of recurrences	Mean recurrence time
Irradiated patients	2	2	12 months
Non-irradiated patients	14	8	57 months

($p = 0.50$)

Regarding the effects of radiotherapy on subsequent recurrences, 7 malignant meningiomas were irradiated at the time of recurrence. The extent of resection immediately preceding radiotherapy was total in 4 and subtotal in 3 cases. Among the 4 totally resected tumours, subsequent recurrences were seen in 2 cases with a mean recurrence interval of 21.5 months. For those patients who underwent complete resection of recurrent tumour without radiotherapy, subsequent recurrences were seen in 4 of 6 cases after an average interval of 23 months (Table 4). This difference was not statistically significant ($p = 0.43$). All 3 recurrent tumours subtotally removed at the time of recurrence were irradiated, and subsequent regrowth occurred in 2 after an average interval of 53 months. Since all patients who had subtotal removal on recurrence were irradiated, no comparison could be made between irradiated and nonirradiated tumours.

Effects of radiotherapy on benign meningiomas: Two benign meningiomas were irradiated after complete excision. The decision for radiotherapy in these cases was based primarily on the inclination of the surgeon. One of these patients died after 3 months and the second was alive at the 5-year follow-up. Among the subtotally removed tumours, 6 were irradiated. Regrowth was seen in 2 of the 6, compared to 26 of 67 nonirradiated tumours. Mean regrowth time was 75 months and 1-, 5-, and 10-year regrowth rates of irradiated lesions were 0%, 20%, and 20%, respectively; mean regrowth time for nonirradiated tumours was 55 months and 1-, 5-, and 10-year regrowth rates were 9%, 38%, and 67%, respectively (Table 5). The difference was not statistically significant ($p = 0.45$). Regarding benign recurrent meningiomas, 3 were irradiated at recurrence and underwent subtotal resection at reoperation (no benign recurrent tumour was irradiated after having undergone complete resection). One of these tumours subsequently regrew after 47 months. In comparison with recurrent tumours subtotally removed at reoperation but not irradiated, regrowth was seen in 5 of 14 cases after a mean interval of 31 months (Table 6). There was no statistical difference between the two groups ($p = 0.22$).

Discussion

Meningiomas comprise 13%–19% of primary intracranial neoplasms[5, 6, 8] and are second only in incidence to gliomas. However, since the early days of neurosurgery these tumours have been characterized by frequent recurrences. Different authors have attempted to find the cause of these high recurrence rates[1,

Table 3. *Malignant Meningiomas.* Effects of radiotherapy after subtotal removal

	Total number	No. of regrowths	Mean regrowth time
Irradiated patients	1	1	14 months
Non-irradiated patients	5	3	10 months

($p = 1.00$)

Table 4. *Malignant Recurrent Meningiomas.* Effects of radiotherapy after total resection of recurrent tumour

	Total number	No. of recurrences	Mean recurrence time
Irradiated patients	4	2	22 months
Non-irradiated patients	6	4	23 months

($p = 0.43$)

Table 5. *Benign Meningiomas.* Effects of radiotherapy after subtotal removal

	Total number	No. of regrowths	Mean regrowth time
Irradiated patients	6	2	75 months
Non-irradiated patients	67	26	55 months

($p = 0.45$)

Table 6. *Benign Recurrent Meningioma.* Effects of radiotherapy after subtotal removal of recurrent tumour

	Total number	No. of regrowths	Mean regrowth time
Irradiated patients	3	1	47 months
Non-irradiated patients	14	5	31 months

($p = 0.22$)

[2, 11, 13, 16], but what Simpson[16] noted 36 years ago holds true today: there is still no agreement on the actual frequency or significance of tumour recurrence.

In our series we found that benign meningiomas tend to occur more frequently in females and malignant tumours more in males. There was no difference between the sexes regarding the potential to recur when benign and malignant meningiomas were studied separately.

Tumour location was also not associated with any statistically significant difference regarding the recurrence potential. It is generally believed that tumour site is correlated with recurrence rates, with basal meningiomas representing the greatest risk[14, 16]. However, these studies have not attempted to separate total resections from subtotally removed tumours. Tumours at certain locations are more difficult to extirpate completely and thus tend to regrow. However, among completely resected tumours, site is not associated with a tendency to recur[11, 12].

The recurrence rate of malignant meningiomas far exceeded that of benign ones. In fact, recurrence was seen in only 2 completely resected benign cases. Ever since Simpson's[16] publication, biological significance of the histologic appearance of meningiomas has been questioned and many believe that prognosis cannot be predicted on the basis of histopathologic analysis[9, 12]. This is merely a representation of the lack of uniformly defined criteria for malignancy. Using the World Health Organization classification criteria, it is possible to define malignant versus nonmalignant with far greater reliability. Another reason why benign meningiomas were found to have a high recurrence rate in earlier studies was that most of the cases reported were treated before the days of operative microscopy. This made it difficult not only to resect lesions completely but also to assess accurately the extent of resection. This drawback was recognized even by those who believed in high recurrence rates of benign meningiomas[13]. Also, since computed tomography was not yet available, no postoperative studies were done to evaluate the extent of tumour removal, which was judged instead solely on the basis of intraoperative observation. All of us are well aware that this can be misleading. In fact, Borovich and Doron[3] found macro- and microscopic clusters of meningothelial cells in the surrounding dura in all patients with meningiomas up to 3 cm from the site of attachment of tumour. Control strips of convexity dura taken from 10 neurosurgical patients without meningioma failed to show such meningothelial islands. They therefore recommended wide resection of dura surrounding the meningioma whenever possible. We support their recommendations.

The efficacy of radiotherapy in controlling the progression of meningiomas remains controversial. Traditionally meningiomas were considered to be radioresistant[7], but radiotherapy has continued to be used mainly because of high recurrence rates. Though regrowth intervals were longer after radiotherapy among benign subtotally removed tumours compared to nonirradiated ones (Tables 4 and 5), this difference was not statistically significant. Among our patients, radiotherapy did not have any benefit in preventing the recurrence, regardless of whether the tumour was benign or malignant or whether radiotherapy was given after first resection or on recurrence. However, our sample size was not large enough to derive any significant conclusions. Carella *et al.*[4] recommended radiotherapy for all malignant and recurrent meningiomas (regardless of extent of resection) and for benign meningiomas removed subtotally at primary resection. This study lacked a control group of nonirradiated patients and important details such as follow-up were absent from the report. Yamashita *et al.*[20] subsequently showed in their series of 7 recurrent meningiomas that radiotherapy given after complete resection of a recurrent tumour has little benefit. It would seem reasonable to consider the use of radiotherapy after subtotal removal, regardless of whether subtotal removal was done at primary resection or reoperation. Wara *et al.*[19] showed that radiotherapy retards tumour progression in incompletely excised meningiomas. Other factors such as the patient's age, medical condition, and extent of residual tumour need to be considered when making the decision. Obviously, the issue is far from being resolved and more experience is necessary to fully evaluate the efficacy of radiotherapy. Unfortunately, there is no study to show any added benefits of radiotherapy for completely resected tumours, but some authors[15] still advocate its use because of the invasive potential of the tumours. In our institution, we no longer use radiotherapy for completely excised meningiomas, whether first or subsequent resection or whether the tumour was benign or malignant. Neither ours nor others' experience has shown any value of radiotherapy for such cases. Regarding the use of chemotherapy, antioestrogens, or antiprogestationals, there are no data to support the benefit of any one of these agents[15, 18]. We do not recommend their use for such purposes.

We believe that recurrence rates in benign meningiomas are far lower than those cited in the literature and that the majority of what has been described as "recurrences"are in fact "regrowths" representing continuous tumour growth after incomplete removal. In fact, whenever recurrence is seen after complete surgical removal, chances are that tumour was atypical or malignant.

References

1. Adegbite AB, Khan MI, Paine KW, Tan LK (1983) The recurrence of intracranial meningiomas after surgical treatment. J Neurosurg 58: 51–56
2. Beks JW, Windt HL (1988) The recurrence of supratentorial meningiomas after surgery. Acta Neurochir (Wien) 95: 3–5
3. Borovich B, Doron Y (1986) Recurrence of intracranial meningiomas: the role played by regional multicentricity. J Neurosurg 64: 58–63
4. Carella RJ, Ransohoff J, Newall J (1982) Role of radiation therapy in the management of meningioma. Neurosurgery 10: 332–339
5. Cushing H, Eisenhardt L (1938) Meningiomas: their classification, regional behavior, life history and surgical end results. Thomas, Springfield, Ill
6. Grant FC (1947) Intracranial meningiomas, surgical results. Surg Gynecol Obstet 85: 419–431
7. Guthrie BL, Carabell SC, Laws ER (1991) Radiation therapy for intracranial meningiomas. In: Al-Mefty O (ed) Meningiomas. Raven, New York, pp 255–262
8. Hoessly GF, Olivecrona H (1955) Report on 280 cases of verified parasagittal meningioma. J Neurosurg 12: 614–626
9. Jellinger K, Slovik F (1975) Histologic subtypes and prognostic problems in meningiomas. J Neurol 208: 279–298
10. Kepes JJ (1990) Review of the WHO's new proposed classification of brain tumours. Proceedings of the XIth International Congress of Neuropathology, Kyoto: 87–97
11. Marks SM, Whitwell HL, Lye RH (1986) Recurrence of meningiomas after operation. Surg Neurol 25: 436–440
12. May PL, Broome JC, Lawry J, Buxton RA, Battersby RDE (1989) The prediction of recurrence in meningiomas. J Neurosurg 71: 347–351
13. Mirimanoff RO, Dosoretz DE, Linggood RM, Ojemann RG, Martuza RL (1985) Meningioma: analysis of recurrence and progression following neurosurgical resection. J Neurosurg 62: 18–24
14. Phillippon J, Cornu P (1991) The recurrence of meningiomas. In: Al-Mefty O (ed) Meningiomas. Raven, New York, pp 87–105
15. Salcman M (1991) Malignant meningiomas. In: Al-Mefty O (ed) Meningiomas. Raven, New York, pp 75–85
16. Simpson D (1957) The recurrence of intracranial meningiomas after surgical resection. J Neurol Neurosurg Psychiatry 201: 22–39
17. Su CF, Shih CJ, Tsou CK, Wang YC (1986) Malignant meningiomas - clinical and pathological study of 10 cases. J Formosan Med Assoc 85: 608–623
18. Waelti ER, Mackwalder TM (1989) Endocrine manipulation of meningiomas with medroxyprogesterone acetate. Effect of MPA on growth of primary meningioma cells in monolayer tissue culture. Surg Neurol 31: 96–100
19. Wara WM, Shelline GE, Newman H, Townsend JJ, *et al* (1975) Radiation therapy of meningiomas. Am J Roentgenol 123: 453–458
20. Yamashita J, Handa H, Iwaki K, Abe M (1990) Recurrence of intracranial meningiomas, with special reference to radiotherapy. Surg Neurol 14: 33–40
21. Zulch KJ (1979) Histologic typing of tumours of the central nervous system. World Health Organization, Geneva

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