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Authors

Fong, Christina
Nagasawa, Daniel T
Chung, Lawrance K
et al.

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Systematic Analysis of Outcomes for Surgical Resection and Radiotherapy in Patients with Papillary Meningioma

Christina Fong[1] Daniel T. Nagasawa[1] Lawrance K. Chung[1] Brittany Voth[1] Nicole Cremer[1] Kimberly Thill[1] Nolan Ung[1] Quinton Gopen[2] Isaac Yang[1]

[1] Department of Neurological Surgery, University of California, Los Angeles, Los Angeles, California, United States
[2] Department of Head and Neck Surgery, University of California, Los Angeles, Los Angeles, California, United State

Address for correspondence Isaac Yang, MD, Department of Neurological Surgery, University of California, Los Angeles, 695 Charles E. Young Drive South, Gonda 3357, Los Angeles, CA 900095-1761, United States (e-mail: iyang@mednet.ucla.edu).

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Abstract

Introduction Papillary meningiomas (PMs) are characterized by their aggressive nature and high rate of recurrence. Due to their rarity, studies examining the relationship between treatment and clinical outcomes for this disease are limited. Gross total resection (GTR) with or without radiotherapy (RT) is considered the standard treatment; however, when GTR is not feasible, subtotal resection (STR) followed by RT may be an effective alternative. In this study, we analyzed the clinical outcomes in patients who either underwent GTR alone, GTR followed by RT, STR alone, or STR followed by RT.

Methods A systematic analysis was performed to identify PM patients with sufficient follow-up and outcome data, as measured by recurrence. Patient data lacking extent of resection, follow-up, or recurrence information were excluded.

Results A total of 29 patients with PM were treated with resections (23 GTRs and 6 STRs).The mean age and mean follow-up of patients in this study were 32.3 years and 42.1 months, respectively. Of these patients, 58.6% experienced recurrence. Overall, 47.8% of patients who underwent GTR experienced recurrence. These patients also demonstrated improved survival compared with STR. Among patients whose tumors were only partially excised, a recurrence rate of 83% was observed.

Conclusion Our results confirm that GTR results in fewer recurrences compared with STR, supporting GTR as the treatment of choice for PM. Furthermore, GTR in conjunction with RT resulted in improved survival compared with GTR alone. When GTR was not feasible, STR with RT was associated with improved survival compared with STR alone. Future studies with more outcome data are needed to elucidate the optimal treatment for this rare disease.

Keywords
- papillary meningioma
- papillary
- meningioma
- surgery
- radiotherapy

Introduction

Meningiomas represent nearly 20% of all primary intracranial tumors.[1,2] Papillary meningiomas (PMs) comprise a mere 2% of meningiomas and is an uncommon but particularly aggressive variant. Due to its rarity, the specific characteristics of this tumor are not well understood. PM is a World Health Organization grade III neoplasm associated with a poor prognosis and a high likelihood of aggressive behavior and recurrence.[1] Although benign meningioma is more prevalent in women, PM is more commonly seen in males and tends to occur in younger patients, frequently seen within the first two decades of life.[2] Some studies report that PM commonly affects children; it is thought to comprise up to 10% of all

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pediatric meningiomas.[3,4] Moreover, PMs exhibit aggressive behavior: 75% of PM lesions demonstrate local invasion into surrounding brain parenchyma.[5] About 55% of patients experience recurrence, and 20% develop distant metastasis through dissemination via cerebrospinal fluid, frequently to the lungs and liver.[1,4–8] Given their destructive nature and propensity for recurrence, the 5-year survival rate of PM is only 40%.[8]

Histopathologically, PM is characterized by a perivascular, pseudopapillary pattern with meningothelial histology in at least part of the tumor.[1] Cyst formation in PM is rare but has been shown to occur in some instances.[3,8,9] PMs are most frequently found in the supratentorial compartment,[10–12] but they can also be found in the posterior fossa, the oculomotor nerve, and the jugular foramen.[3,13–16] PMs may have any of the following features on computed tomography scanning and magnetic resonance imaging: irregular tumor shape, heterogeneous enhancement with gadolinium, tumor invasion into adjacent brain structures, and a high MIB-1 index.[12,16,17] However, because these characteristics are nonspecific, the distinction between PM and other lesions cannot be reliably determined through imaging alone.

Symptoms seen in PM patients include headache, vomiting, and blurred vision. Typical signs seen in pediatric PM patients may include symptoms related to increased intracranial pressure and various neurologic deficits such as limb or cranial nerve palsy.[3,8] Studies show that both intracranial pressure and related symptoms were reduced in severity following surgical treatment.[3,8,10]

The current standard of care for all types of meningioma is surgical resection which has been shown to be associated with lower rates of recurrence.[3,17,18] Furthermore, surgical resection provides symptomatic relief by lessening the mass effect, and it allows for diagnostic pathologic sampling. The primary means of treating malignant meningioma is aggressive surgical management as well. Gross total resection (GTR) provides patients with increased disease-free survival and fewer recurrences.[18] However, when GTR is not feasible, subtotal resection (STR), subtotal resection followed by radiotherapy (RT) or repeat surgery for recurrence may be necessary.[18–20] In a study of 20 patients with recurrent meningioma, a median radiation dose of 59.4 Gy was able to achieve a 47% 5-year survival rate with no serious complications associated with RT.[21] In another study based on a retrospective analysis of 140 benign and malignant intracranial meningiomas, Goldsmith et al suggested that STR and RT may be able to achieve progression-free survival rates comparable with that of GTR in meningioma patients.[21]

Although research analyses are currently available for all meningiomas or all malignant meningiomas, studies specifically addressing PM are uncommon. Specific characteristics of PM are not well known due to the limited number of PM case reports available in the literature. Studies examining the relationship between treatment and clinical outcomes for this disease are similarly limited. Moreover, analyses of PM management are further complicated by unknown factors, such as the specific extent of surgical resection or the presence of recurrence in patients. Therefore, there is no clear conclusion regarding the proper surgical and postoperative treatment specifically for PM.[1,2,5] Given the aggressive clinical behavior of PM, better knowledge regarding the proper course of treatment is vital to decreasing the morbidity and mortality in these patients. The goal of this study was to determine the treatment modality with the most improved clinical outcome, particularly for patients with the rare diagnosis of PM. More specifically, we analyzed the clinical outcomes in patients who either underwent GTR alone, GTR followed by RT, STR alone, or STR followed by RT.

Methods

A comprehensive literature review was performed to identify PM patients with follow-up and outcome data, as measured by recurrence and survival at time of follow-up. An online literature search was performed in August 2013 for all published articles regarding PM using the keywords "papillary AND meningioma." A total of 21 relevant articles or abstracts ($n = 47$) were identified and available. An extensive review was performed to extract clinical data on patient age, sex, tumor location, treatment algorithm, pathology reports, recurrence, metastases, and follow-up. Outcomes were extracted and compiled into a single database.

Inclusion criteria were (1) PM as the primary diagnosis, (2) available data regarding treatment modality, and (3) available data on recurrence and/or metastases. A total of 18 patients were excluded from this study due to lack of information regarding extent of resection, follow-up time, or recurrence information.[12,16]

The cases with sufficient data ($n = 29$) were separated into two groups: those who underwent GTR and those that underwent STR.[3,4,6–11,14,15,18,23–29] These initial groups were further subdivided into those that received GTR only in addition to STR only and those that received STR in addition to RT. Data were aggregated and analyzed using Microsoft Excel. Survival data were depicted using Kaplan-Meier survival curves generated from Microsoft Excel.

Results

Total Population

A total of 29 patients with the diagnosis of PM met the inclusion criteria. Thirteen male patients (44.8%) and 16 female patients (55.2%) were included in this study. The average reported age of patients in this study was 32.3 years (male: 30.7 years; female: 33.6; range: 2.6–74 years), with an average follow-up of 42.1 months. The patients' tumors were most commonly histologically characterized by the presence of papillary structures surrounding the vasculature, mitotic figures, and invasion into the brain.

Of the 29 patients, 58.6% experienced recurrence, 8 of whom (28%) developed distant metastases, most commonly to the lungs. All patients in this study were initially treated with surgical resection. GTR was achieved in 23 patients (79%), 4 of whom additionally underwent postoperative RT. The remaining six patients (21%) underwent STR, three of whom underwent postoperative RT.

Gross Total Resection versus Subtotal Resection Recurrence

The presence of recurrence in patients treated with GTR and STR is presented in ►**Table 1**. Overall, 47.8% of patients who underwent gross total resection of the tumor with or without RT experienced recurrence. Overall, 83% of patients who underwent STR with or without RT experienced recurrence.

The PM lesion was totally excised without RT in 19 patients. Nine of these patients (47%) experienced local recurrence or metastasis of the tumor. Four patients underwent GTR followed by postoperative fractionated RT with an average of 40.5 Gy. Of these patients, two of four experienced recurrence (50%).

Tumors were partially removed without RT in three patients. Two of these experienced recurrence (67%). Of the three patients who received STR in addition to fractionated RT (average: 49.5 Gy), all three experienced recurrence or metastases (100%).

Gross Total Resection versus Subtotal Resection Survival

Survival outcomes were depicted using Kaplan-Meier survival curves generated with Microsoft Excel. GTR of the tumor displayed a trend towards an association with improved survival outcomes, compared with STR (►**Fig. 1**). Furthermore, patients who underwent GTR and RT appeared to have better survival than patients receiving GTR alone (►**Fig. 2**). These differences were not statistically significant. Survival curves comparing subtotal resection with and without RT could not be generated due to insufficient data.

Discussion

PMs are rare tumors comprising $<$ 5% of all meningiomas.[1,2] This study examined a database of 29 PM patients with data compiled from 21 case studies and retrospective reviews from 1978 through 2012. Although some data were not included due to lack of critical information, our analysis represents one of the largest studies examining treatment outcomes of PM lesions.

The current literature has shown that whereas most meningiomas occur predominantly in females between the ages of 50 and 79,[15] PM most commonly occurs in males and with an average age of 35 years.[3] Our study demonstrated a male-to-female ratio of 0.8, with an average age of 32.3 years. This discrepancy in the gender ratio with the current literature may be due to the exclusion of patient data lacking information regarding the extent of surgical resection. Notably, of the 29 patients, our study included 9 children/adolescents with PM, ranging from ages 2.6 to 19 years.

Studies of malignant meningiomas suggest that GTR provides better outcomes, whereas subtotal excision is associated with greater recurrence.[18,21] However, significant data specifically regarding PM are not widely available. Our analysis suggests that overall, GTR in PM patients results in reduced recurrences compared with that after a STR (47.8% in GTR and 83.3% in STR), supporting GTR as the treatment of choice for PM (►**Table 1**). GTR in combination with RT displayed a trend towards improved survival rates when compared with gross

Table 1 Recurrence in GTR, GTR and RT, STR, and STR and RT cohorts for papillary meningioma

	No. of patients	No. of recurrences	Incidence of recurrences, %
GTR	19	9	47.37
GTR RT	4	2	50.00
STR	3	2	66.67
STR RT	3	3	100.00

Abbreviations: GTR, gross total resection; RT, radiotherapy; STR, subtotal resection.

Patients treated with GTR and patients treated with GTR and RT had the lowest incidence of recurrences, compared with patients treated with STR.

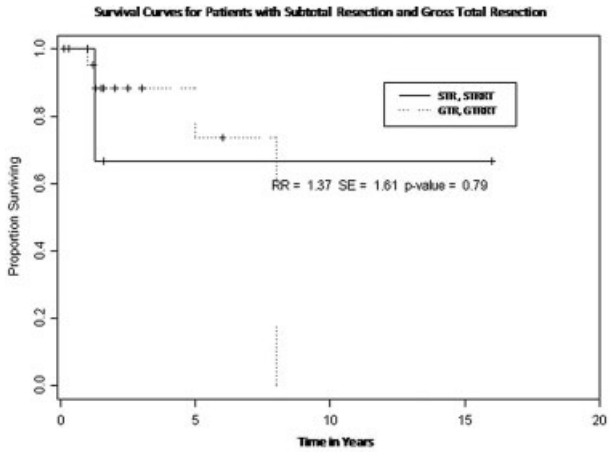

Fig. 1 Survival curves comparing gross total resection (GTR) with and without radiotherapy (RT) versus subtotal resection (STR) with and without RT. Patients who underwent GTR with and without RT displayed a trend towards better survival outcomes than patients who underwent STR with or without RT. This difference was not statistically significant.

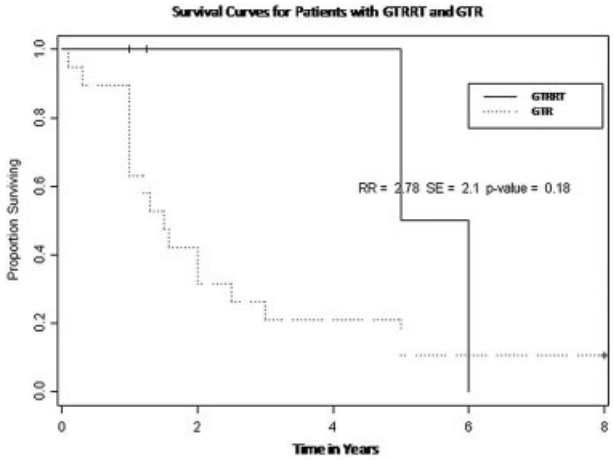

Fig. 2 Survival curves comparing gross total resection (GTR) and radiotherapy (RT) versus GTR alone. Data from patients who underwent both GTR and RT suggested an improved survival when compared to patients who underwent GTR alone. This difference was not statistically significant.

total tumor resection alone. When total surgical removal of the tumor was not feasible, STR with or without RT were the most commonly used treatments; both of these treatment modalities were associated with increased numbers of recurrence and/or metastases compared with complete surgical removal. STR in conjunction with RT was associated with improved overall survival compared with STR alone. These associations were not statistically significant, likely due to the small sample size; however, they are consistent with more generalized malignant meningioma reports in the literature regarding the effectiveness of RT in cases when STR is necessary.[19,20]

This study was limited by low statistical power due to the rarity of PM cases, incomplete data inherent in a retrospective review, varied baseline patient characteristics, and variation in the treatments. Overall, 18 of the initial 47 cases were excluded from this study, largely due to the absence of data regarding extent of surgical resection. Given the small sample size, this sampling bias may have altered the results of this study. Therefore, future studies with more thorough outcome data are needed to further analyze the optimal treatment for this rare disease.

Conclusion

This study analyzed 29 incidences of PM documented in the literature. Based on the available data, GTR with or without RT was associated with reduced recurrences and improved survival compared with STR with or without RT in patients with PM. We also found that GTR with RT appeared to be associated with improved survival compared with GTR alone, although limited data prevented a meaningful analysis. Likewise, STR with RT was associated with improved survival compared with STR alone. The incomplete data and low incidence of this disease limited our comparisons of recurrence and survival with the various treatments. Although a larger prospective study in the future would be more ideal to control for confounding variables, the rarity of this disease makes this difficult to accomplish. Therefore, given the available data, our study provides valuable information regarding the optimal treatment protocol for patients diagnosed with PM.

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