Proposed Treatment for Intracranial Transitional Meningioma: A Single-Center Series of 298 Cases

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■ OBJECTIVE: **We retrospectively assessed the surgical outcomes of transitional meningioma (TM) in a relatively large series to evaluate the long-term outcomes and propose an appropriate treatment strategy for TM.**

■ METHODS: **We included 298 patients who had undergone surgery from September 2011 to August 2013. The clinical characteristics, surgical record, and follow-up data for these patients were retrieved.**

■ RESULTS: **The 298 enrolled patients included 213 women (71.5%). The mean and median age of the 298 patients was 50.7 ± 0.6 years and 52.0 years (range, 6.0–74.0), respectively. Radiologically, 144 tumors (48.3%) were located in the skull base. Gross total resection (GTR) was achieved in 266 patients (89.3%); 7 patients (2.6%) received adjuvant radiotherapy. After a median follow-up of 61.8 months, 23 patients (8.6%) had developed recurrence and 2 patients (0.8%) had died. The results from univariate analysis indicated that GTR was associated with better progression-free survival (hazard ratio, 0.165; 95% confidence interval, 0.071–0.382; $P < 0.001$).) Skull base tumors tended to predict for poor progression-free survival (hazard ratio, 2.169; 95% confidence interval, 0.919–5.118; $P = 0.077$). For the first tumor recurrence, 11 patients (47.8%) underwent gamma knife radiosurgery, and only 2 patients developed a second recurrence.**

■ CONCLUSION: **The results from the present study have shown that GTR should be achieved during the first surgery for TM. Gamma knife radiosurgery might be an effective therapy for patients with tumor recurrence.**

INTRODUCTION

Meningiomas are the most common primary brain tumors and account for ~30% of brain neoplasms.[1] These tumors originate from arachnoid cap cells or arachnoid trabeculae and have been classified into 3 grades and 15 different variants by the World Health Organization (WHO) 2016 classification.[2] Transitional meningioma (TM) is an uncommon benign meningioma. Pathologically, TM is characterized by a transitional morphological appearance between endothelial meningiomas and fibrous meningiomas and will often be solitary. Despite the increasing understanding of grade I meningiomas from many previous reports, the reported data on this subtype remain scarce. In the present study, we retrospectively assessed the surgical outcomes, evaluated the risk factors, and drew conclusions regarding the proposed treatment strategy for TM in a relatively large series.

METHODS

We used a retrospective case database from our center and pathological records to identify patients who had undergone TM surgery from September 2011 to August 2013. Pathology reports indicating a diagnosis of TM were used to define the patients included in our study. As a result, 298 patients with TM were

Key words
- Gross total resection
- Proposed treatment
- Transitional meningioma

Abbreviations and Acronyms
EOR: Extent of resection
GTR: Gross total resection
KPS: Karnofsky performance scale
MRI: Magnetic resonance imaging
PFS: Progression-free survival
STR: Subtotal resection
TM: Transitional meningioma
WHO: World Health Organization

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eligible for analysis. The Beijing Tiantan Hospital research ethics committee approved the present study.

The clinical information regarding patient gender, age at operation, previous treatment, preoperative Karnofsky performance scale (KPS) score, surgical approach, tumor consistency, tumor location, tumor size, contrast enhancement on magnetic resonance imaging (MRI), and extent of resection (EOR) was collected. The tumor location was divided into 2 major categories: skull base (i.e., anterior fossa, petroclival region, sphenoid ridge, cerebellopontine angle, foramen magnum) and nonskull base (i.e., convexity, falx, parasagittal, tentorial, pineal region, intraventricular area). The tumor consistency was classified into 3 categories: soft/crisp, tenacious, and solid.

A preoperative MRI examination was routinely performed (Figure 1), which included T1-weighted imaging, T2-weighted imaging, and T1-weighted imaging with contrast enhancement (administered with gadolinium). Otherwise, a computed tomography scan was used to evaluate the tumor. The tumor size was evaluated according to the maximum tumor diameter. Peritumoral edema was assessed on T2-weighted MRI. The pattern of contrast enhancement was divided into homogeneous and heterogeneous. The EOR was determined from a postoperative MRI study and was

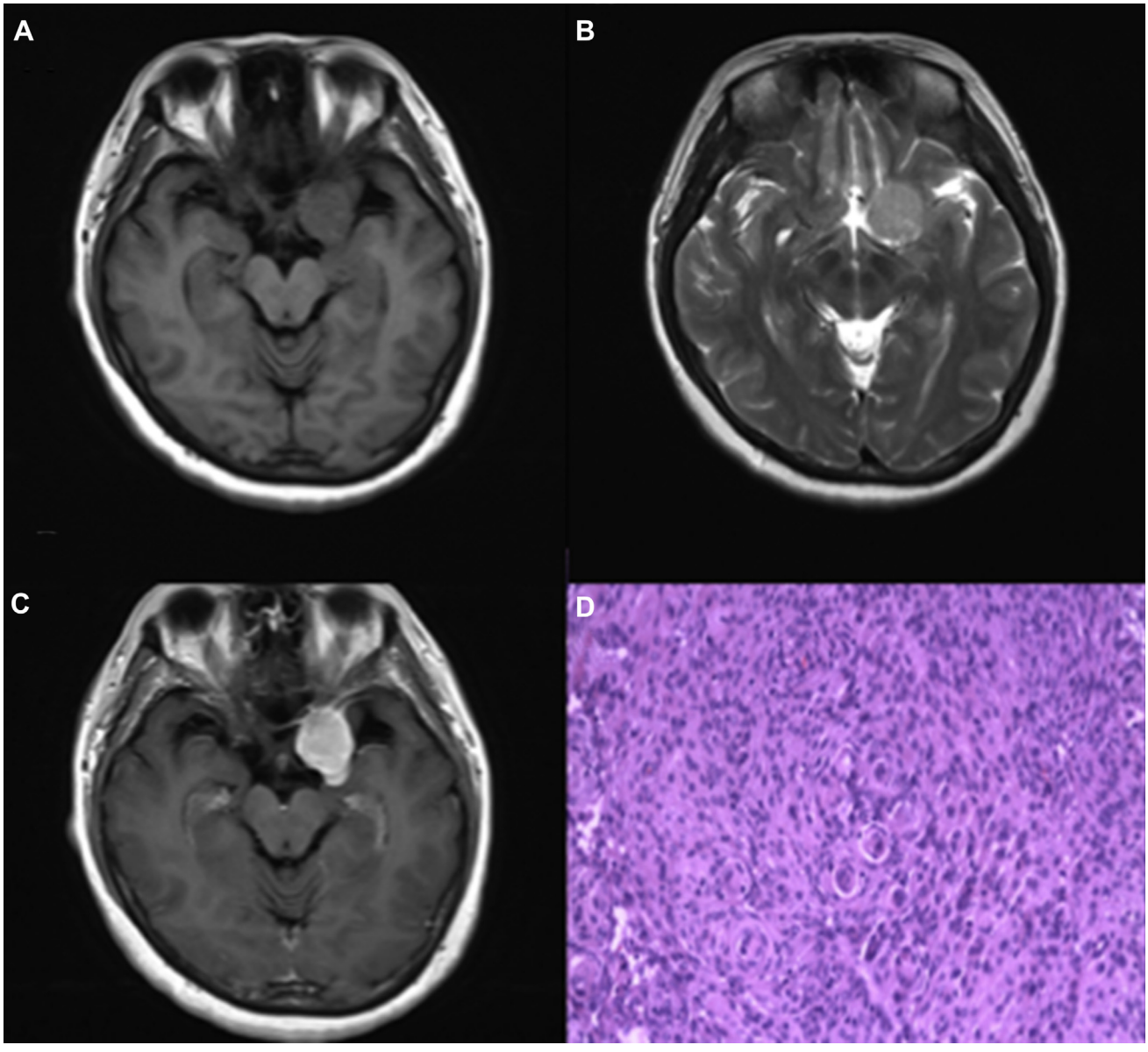

Figure 1. A 48-year old woman with transitional meningioma located in the parasella. Magnetic resonance images showing (**A**) hypointensity on T1-weighted, (**B**) isointensity on T2-weighted, and (**C**) homogeneous enhancement. (**D**) Pathologic examination revealed the diagnosis of transitional meningioma.

divided into 2 categories: GTR (without any residue) and subtotal resection (STR) (with tumor residue).

Surgical Outcomes and Follow-Up

Follow-up data after surgery were accessible for 266 patients (89.3%) with TM. Twenty-five patients had been lost to follow-up. At the end of the study, 5 patients had died during surgery and 2 patients had died of additional diseases other than TM. At the final follow-up examination, the KPS score, postoperative radiation data, and treatment strategies at recurrence were recorded. An evaluation of the patients' postoperative KPS scores was performed during the clinic visits. Tumor progression, defined as an increase in diameter of 2 mm, was recorded by comparing the preoperative and last follow-up MRI evaluation. Progression-free survival (PFS) was defined as the duration between surgery and tumor progression. Follow-up information was obtained during outpatient visits or by telephone review.

Statistical Analysis

A descriptive analysis of the population was performed using IBM SPSS, version 21.0 (IBM Corp., Armonk, New York, USA), for Windows. Adverse predictors for a poor outcome were evaluated by univariate analysis. A paired samples t test was used to compare the preoperative and postoperative and preoperative and follow-up KPS scores, respectively. Survival curves were generated using the Kaplan-Meier method. Statistical significance was considered present at $P < 0.05$.

RESULTS

Clinical Characteristics

Of the 298 patients, 85 were men (28.5%) and 213 were women (71.5%). The mean and median age of the 298 patients was 50.7 ± 0.6 and 52.0 years (range, 6.0–74.0), respectively. Of the 298 patients, 19 (6.4%) had previously undergone treatment before admission to our hospital. Of these 19 patients, 12 (4.0%) had undergone surgery, 6 (2.0%) had undergone surgery with adjuvant radiotherapy and 1 (0.3%) had undergone ventriculoperitoneal shunt placement. The median preoperative KPS score was 90 (range, 70–100). Most patients presented with initial manifestations due to a mass effect. These included headache (n = 98; 32.9%), dizziness (n = 66; 22.1%), seizures (n = 22; 7.4%), upper or lower limb numbness (n = 21; 7.0%), upper or lower limb weakness (n = 46; 15.4%), visual disturbance (n = 48; 16.1%), hyposmia (n = 5; 1.7%), hearing loss (n = 16; 5.4%), and ataxia (n = 13; 4.4%). The diagnosis of TM was incidental from an MRI scan for 34 patients (11.4%). The clinical characteristics of the entire cohort are summarized in Table 1.

Table 1. Summary of Patient Characteristics

Characteristic	Value
Overall	298
Gender	
Male	85 (28.5)
Female	213 (71.5)
Age (years)	
Range	6.0–74.0
Mean	50.7 ± 0.6
Median	52.0
Previous treatment	
Surgical resection	12 (4.0)
Surgical resection plus radiotherapy	6 (2.0)
Ventriculoperitoneal shut	1 (0.3)
Preoperative KPS score	
100	34 (11.4)
90	150 (50.3)
80	73 (24.5)
70	41 (13.8)
Mean	86
Median	90
Clinical symptoms	
Headache	98 (32.9)
Dizziness	66 (22.1)
Seizure	22 (7.4)
Upper or lower limb numbness	21 (7.0)
Upper or lower limb weakness	46 (15.4)
Visual disturbance	48 (16.1)
Hyposmia	5 (1.7)
Hearing loss	16 (5.4)
Unsteady gait	13 (4.4)
Physical examination	34 (11.4)

Data presented as number of patients, mean ± standard deviation, or *n* (%).
KPS, Karnofsky performance scale.

Radiologic Characteristics

Of the 298 patients in the present cohort, 154 (51.7%) had presented with nonskull base tumors, including convexity (n = 103; 34.6%), falx (n = 19; 6.4%), parasagittal (n = 10; 3.4%), tentorial (n = 13; 4.4%), pineal region (n = 2; 0.7%), and intraventricular area (n = 7; 2.3%). The remaining 144 patients (48.3%) had presented with tumors originating from the skull base. Of these 144 patients, 59 (19.8%) had tumors based in the anterior fossa, 28 (9.4%) had tumors based in the petroclival region, 23 (7.7%) in the sphenoid ridge, 19 (6.4%) at the cerebellopontine angle, and 15 (5.0%) had tumors based in the foramen magnum. Preoperative MRI studies were available for 283 patients (95.0%). The tumors exhibited radiological heterogeneity, including hypointense in 190 (67.1%), isointense in 87 (30.8%), and hyperintense in 6 (2.1%) on T1-weighted MRI and hypointense in 4 (1.4%), isointense in 51 (18.0%), and hyperintense in 228 (80.6%) on T2-weighted MRI. Homogeneous (n = 215; 76.0%) and heterogeneous contrast enhancement (n = 68; 24.0%) was identified on the preoperative MRI studies. Peritumoral edema was observed in 113 patients

(39.9%), and the tumor shape for 255 (90.1%) was regular. The median maximal diameter was 3.7 cm (range, 1.3–8.5). The radiologic data are summarized in Table 2.

Surgical Findings and Outcomes

A spectrum of surgical approaches was performed for each case. The tumor had presented as soft/crisp in 55 cases (18.5%), tenacious in 194 (65.1%), and solid in 49 cases (16.4%). GTR was achieved in 266 patients (89.3%) and STR in 32 (10.7%). The GTR rate for the nonskull base and skull base tumors was 92.1% and 85.0%, respectively. Surgical complications occurred in 61 patients (20.5%). Intracranial infections occurred in 32 patients (10.7%). Cranial nerve neuropathy ($n = 17$; 5.7%) was the most common morbidity, followed by intracranial hematoma ($n = 7$; 2.3%), hydrocephalus requiring a ventriculoperitoneal shunts ($n = 3$; 1.0%) and cerebrospinal fluid leakage ($n = 3$; 1.0%). Additionally, pneumonia developed in 7 patients (2.3%). Five patients died nearly 1 month ($n = 2$), 28 days ($n = 1$), 1.5 months ($n = 1$), and 2 months ($n = 1$) after surgery as a result of delayed hematomas ($n = 2$), seizure ($n = 1$), cerebral infarction ($n = 1$), and cerebrospinal fluid leak with intracranial infection ($n = 1$). The mean postoperative KPS score at discharge was 78 (range, 0–100). The mean postoperative KPS scores had significantly decreased after surgery at discharge compared with the mean preoperative KPS score (78 vs. 86; $P < 0.001$, paired samples t test). The data are summarized in Table 3.

Follow-Up Outcome

The median follow-up period was 61.8 months (range, 11.7–77.5). Only 7 patients (2.6%) received adjuvant radiotherapy. The mean and median KPS scores for the 266 patients was 91 and 95 (range 0–100), respectively. At the end of the follow-up period, 23 patients (8.6%) had developed a recurrence, and 2 patients (0.8%) had died of tumor progression. The estimated mean PFS was 73.8 months, and the 1-, 3-, and 5-year PFS rates were 99.2%, 95.5%, and 92.4%, respectively. The follow-up KPS score was significantly higher compared with the postoperative KPS (91 vs. 78; $P < 0.001$, paired samples t test; Table 4).

Parameters and Outcomes

The patients who had received GTR during surgery had a significantly longer mean PFS (75.9 months) than those who had received STR (59.9 months; $P < 0.001$, log-rank test). The mean survival of the patients with nonskull base tumors (73.8 months) was marginally longer than that of patients with skull base tumors (72.0 months), although the difference between tumor location and survival was not statistically significant ($P = 0.07$, log-rank, test). On univariate analysis, no significant association was observed between the other factors (preoperative KPS score, patient age, tumor size, peritumoral edema, contrast enhancement on MRI) and PFS (Table 5).

Salvage Treatment at Recurrence

Of the 23 patients with a first recurrence, 19 received various treatments, including reoperation in 8 (34.8%) and gamma knife radiosurgery in 11 (47.8%). However, 4 patients (17.4%) declined

Table 2. Radiographic Characteristics

Characteristic	*n* (%)
Location	
Nonskull base	154 (51.7)
Convexity	103 (34.6)
Falx	19 (6.4)
Parasagittal	10 (3.4)
Tentorial	13 (4.4)
Pineal region	2 (0.7)
Intraventricular area	7 (2.3)
Skull base	144 (48.3)
Anterior fossa	59 (19.8)
Petroclival region	28 (9.4)
Sphenoid ridge	23 (7.7)
Cerebellopontine angle	19 (6.4)
Foramen magnum	15 (5.0)
T1-weighted imaging*	
Hypointense	190 (67.1)
Isointense	87 (30.8)
Hyperintense	6 (2.1)
T2-weighted imaging*	
Hypointense	4 (1.4)
Isointense	51 (18.0)
Hyperintense	228 (80.6)
Enhancement*	
Homogeneous	215 (76.0)
Heterogeneous	68 (24.0)
Peritumoral edema*	
Present	113 (39.9)
Absent	
Tumor boundary*	
Clear	260 (91.9)
Unclear	23 (8.1)
Tumor shape*	
Regular	255 (90.1)
Irregular	28 (9.9)
Maximum tumor size (cm)*	
Range	1.3–8.5
Mean	3.9
Median	3.7

*Preoperative magnetic resonance imaging scans were not available for 15 patients (5.0%).

Table 3. Surgical Findings and Outcomes for 298 Patients at Discharge

Characteristic	*n* (%)
Surgical approach	
Ipsilateral or bilateral subfrontal	78 (26.2)
Frontotemproal	51 (17.1)
Frontoparietal	43 (14.4)
Combined supratentorial/infratentorial	33 (11.1)
Anterior transpetrosal	21 (7.0)
Retrosigmoid	16 (5.4)
Fronto-orbitozygomatic	13 (4.4)
Far lateral	12 (4.0)
Subtemporo-occipital	9 (3.0)
Presigimoid	7 (2.3)
Posterior suboccipital midline	7 (2.3)
Temporoparietal	4 (1.3)
Transnasosphenoidal	3 (1.0)
Trans-supraorbital	1 (0.3)
Tumor consistency	
Soft/crisp	55 (18.5)
Tenacious	194 (65.1)
Solid	49 (16.4)
Extent of resection	
Gross total resection	266 (89.3)
Subtotal resection	32 (10.7)
Complications	61 (20.5)
Cranial nerve neuropathy	17 (5.7)
Intracranial infection	32 (10.7)
Intracranial hematoma	7 (2.3)
Hydrocephalus	3 (1.0)
Cerebrospinal fluid leak	3 (1.0)
Pneumonia (additional)	7 (2.3)
Surgical mortality	5 (1.7)
KPS score at discharge	
80—100	208 (69.8)
60—70	74 (24.8)
0—50	16 (5.4)
Mean	78
Median	80

KPS, Karnofsky performance scale.

any treatment for their first recurrence. Of the 15 patients with skull base TM, 7 underwent gamma knife radiosurgery, 4 (17.4%) underwent received surgery, and 4 (17.4%) chose observation. Of these 23 patients, 11 developed a second recurrence. The major treatment regimens for the second salvage therapy were as follow: 3 patients (27.3%) underwent surgery plus gamma knife radiosurgery, 2 patients (18.2%) underwent surgery alone; and 2 patients (18.2%) underwent gamma knife radiosurgery (Figure 2).

Table 4. Outcomes for 266 Patients at Final Follow-Up Visit

Characteristic	*n* (%)
Gender	
Male	76 (28.6)
Female	190 (71.4)
Follow-up symptoms	
Headache	12 (4.5)
Dizziness	4 (1.5)
Upper or lower limb numbness	4 (1.5)
Upper or lower limb weakness	10 (3.8)
Visual disturbance	24 (9.0)
Adjuvant radiotherapy	7 (2.6)
Lost to follow-up	25 (9.4)
Follow-up duration (months)	
Range	11.7—77.5
Mean	61.8
Median	63.3
KPS score at final follow-up visit	
0	2 (0.8)
70—80	84 (31.6)
90—100	180 (67.6)
Mean	91
Median	95
Recurrence	23 (8.6)
Death	2 (0.8)

DISCUSSION

Because of the relative infrequency and benign nature of intracranial TMs, to the best of our knowledge, no studies on TM have been reported. The aim of the present study was to estimate the short- and long-term treatment outcomes for patients with TM treated with surgical resection. In addition, the clinical features, radiologic characteristics, and factors affecting survival were recorded.

Parameters and Survival

Similar to the other subtypes of WHO grade I meningiomas, a female predominance (71.5%) was also identified in patients with TMs. Female gender is a potential risk factor related to benign meningiomas because of their common expression of progesterone receptors.[3] According to the radiological findings, most TMs

Table 5. Prognostic Factors on Univariate Analysis for 266 Transitional Meningiomas

	Progression-Free Survival		
Variable	***P* Value**	**HR**	**95% CI**
Male gender	0.224	0.513	0.174—1.507
Preoperative KPS per 10-point increase	0.346	0.978	0.934—1.024
Age per 1-year increase	0.568	0.989	0.954—1.026
Skull base	0.077	2.169	0.919—5.118
GTR	0.000*	0.165	0.071—0.382
Maximum diameter per 0.1-cm increase†	0.744	0.953	0.715—1.271
Peritumor edema†	0.523	0.746	0.304—1.831
Heterogeneous†	0.522	0.702	0.237—2.073

PFS, progression-free survival; HR, hazard ratio; CI, confidence interval; KPS, Karnofsky performance scale; GTR, gross total resection.
*Statistically significant.
†Data from 253 patients were available.

presented as hypointense on T1-weighted MRI, and the tumors were commonly hyperintense on T2-weighted MRI. The radiological features of TM were not distinctively different from those of the other subtypes of meningiomas. Thus, pathological examination might be key for the differential diagnosis. The presence of peritumoral edema and contrast enhancement on MRI (homogeneous enhancement vs. heterogeneous enhancement) have been reported to be a predictor in previous studies.[4,5] However, no significant relationship was observed between these factors and the outcomes in our study. Also, the present study failed to find that better local control was associated with a smaller tumor size. However, the larger tumors caused a greater mass effect and often adhered to the neurovascular structure more tightly, which could increase the risk of surgical morbidity. Tumor location was not significantly related to PFS in our cohort; however, the patients with skull base TMs tended to have poor PFS. Additionally, tumor location should be an important consideration when determining the surgical management strategies. Skull base tumors will frequently be adherent to critical neurovascular tissue, which has been associated with greater surgical complication rates. Thus,

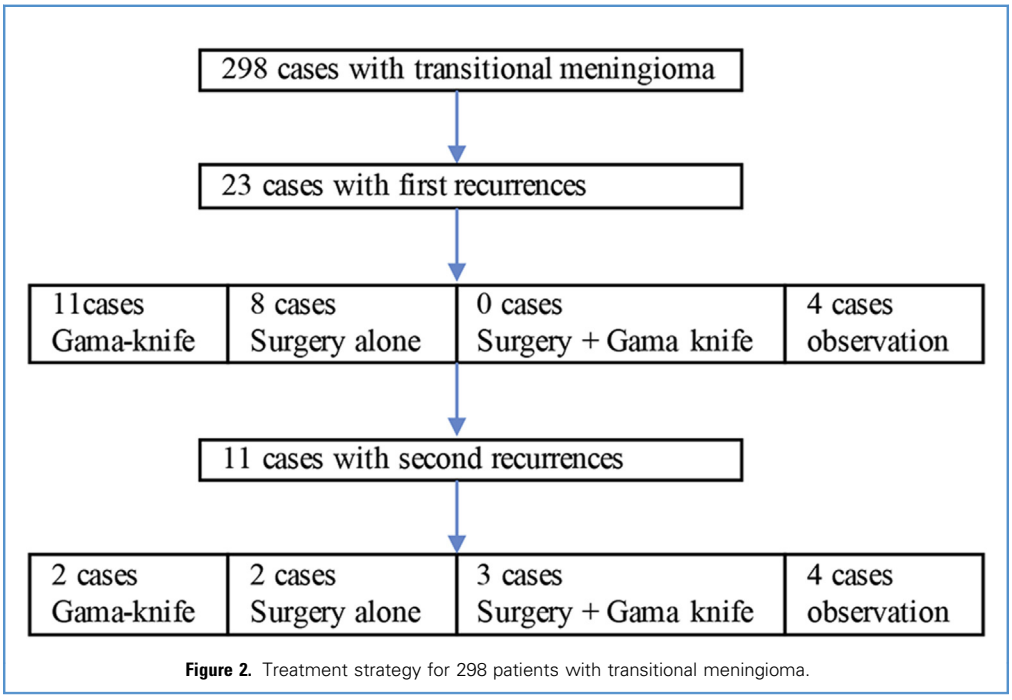

Figure 2. Treatment strategy for 298 patients with transitional meningioma.

completely removing skull base tumors has commonly been regarded as challenging.

EOR and Outcome

Complete resection is the optimal surgical management for these benign meningiomas. In our case series, significantly better PFS was identified in the GTR subgroup. However, the potential damage in neurologic function should be considered during the treatment course because the initial goal of treatment for WHO grade I meningiomas is to prevent location-related symptoms. Especially for tumors on the skull base, severe complications, such as cranial nerve neuropathies, intracranial infections, and the cerebrospinal fluid leaks, were common. It was difficult to achieve GTR for skull base TMs. In our study, a skull base location was not a statistically significant predictor for worse PFS; however, GTR significantly prolonged the PFS, probably indicating that the differences in tumor behavior associated with a skull base location influenced the outcome. These observations could have accounted for the EOR achieved.

Overall, complications were observed in 61 patients (20.5%). However, statistically significant improvements were observed when comparing the follow-up KPS score with the postoperative KPS score. Patients with a surgical treatment history have not usually been considered suitable surgical candidates because of the greater surgical risk from a second procedure.[6] Therefore, achieving the maximal tumor resection at the first operation is critical for those patients to achieve a favorable prognosis in the long term. Regardless of the EOR or tumor location, the surgical complication rates ranged from 20% to 72.7% in previous studies.[7-10] The goal of complete tumor resection should be weighed against the risk of surgical morbidities.

Proposed Treatment Strategy

TM is a subtype of benign meningioma with an unexpectedly high recurrence rate, whose prognostic factors and surgical outcomes have not been previously described. Thus, little evidence is available to guide the decision for the prevention of tumor recurrence and the optimal treatment at recurrence. An increasing number of patients have accepted observation or gamma knife radiosurgery as the primary treatment either because of a small tumor size or because they had presented without symptoms. However, these treatments cannot provide a definitive histological diagnosis, and we could not differentiate between benign and nonbenign meningiomas on the preoperative MRI studies. Thus, we recommended to patients that the appropriate treatment was surgery, which could achieve intracranial decompression, obtain maximal safe cytoreduction, and contribute to the success of subsequent radiation (if the tumor was malignant or a residual lesion was present, especially at the skull base). However, we did not intend to sacrifice neurological function to achieve radical tumor removal. From the findings of other studies, radiosurgery has been recommended as an appropriate treatment for residual tumors,[11] and surgery combined with immediate radiosurgery was related to better PFS.[12]

In addition, in our cohort, gamma knife radiosurgery was increasingly performed for the first recurrence of TM. Eleven patients underwent gamma knife radiosurgery for their relapse, including 7 patients with skull base tumors. This strategy is usually used for recurrent skull base TMs, which are difficult to resect.[13,14] Our study showed that of the 4 patients who had undergone observation, 2 died. Although we were not able to perform a statistical analysis of the treatment for the recurrent tumors, patients with tumor recurrence should actively accept effective treatment and not chose observation. Future studies are needed to further prove this.

Study Limitations

The present study was a retrospective review of a benign and relatively rare tumor; thus, a potential bias existed. The short clinical follow-up period was inadequate for a thorough evaluation of recurrence of this benign meningioma. We were unable to evaluate the association between the different treatments at recurrence and outcomes because of the small cohort size. However, the present study is still the only study to have focused on TMs, and our findings offer considerable value toward understanding the clinical characteristics of this tumor and guiding neurosurgeons in choosing the optimal treatment strategy for patients with TM.

CONCLUSION

Complete resection is a favorable factor for PFS in patients with TM. It is rational to recommend that GTR should be achieved during the first treatment of TM, if it can be accomplished with minimal morbidity. Gamma knife radiosurgery could be an effective therapy at the first recurrence of TM.

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