Management of Recurrent Trigeminal Neuralgia Associated with Petroclival Meningioma

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Abstract

Objective Petroclival meningioma (PM) presents with trigeminal neuralgia (TN) in < 5% of cases. Neurosurgeons often face the dilemma of formulating a treatment protocol when TN recurs. In this study, we sought to set up a protocol in patients with PM who had a recurrent TN.

Materials and Methods We performed a retrospective review of 57 patients with PM. Of the 57 patients, only 7 patients presented with TN, and six patients experienced recurrent TN. The study population was evaluated clinically and radiographically after treatment.

Results Overall improvement of pain control after various treatments was 67%, and tumor control was 100%. The pain-free period was 2 years for the Gamma Knife radiosurgery (GKRS) group and 4 years for the resection group when treated as a primary treatment ($p = 0.034$). Of the six patients, four patients had Barrow Neurosurgical Institute (BNI) score I (no TN, no medication), and two patients had BNI score III (some pain controlled with medication). The Karnofsky performance scale score was significantly improved after treatment compared with the pretreated status (78 versus 88; $p = 0.044$).

Conclusion Microsurgical resection is superior to GKRS in achieving and maintaining pain-free status in patients with recurrent trigeminal pain associated with PM.

Keywords

- petroclival meningioma
- recurrent trigeminal neuralgia
- management
- outcome

Introduction

Intracranial tumors involving the trigeminal nerve lead to an unusual but important cause of trigeminal neuralgia (TN), or tic douloureux. About 5.6% of patients with posterior fossa tumor can present with TN.¹ A century ago, the association of TN with cerebellopontine angle meningioma was first reported by Weisenburg et al.² Subsequently, several cases of TN secondary to intracranial tumor were described.^{2–4} Petroclival meningiomas (PMs) can present with TN as well because of their intimate relationship to the trigeminal nerve. Although multiple case reports have addressed this issue in the literature, a case series is lacking that points toward the rarity of this entity. Current approaches of treatment for

tumor-related TN include tumor removal with or without microvascular decompression,^{3,5} radiosurgery,^{6,7} rhizotomy,^{8,9} and percutaneous balloon decompression.^{10,11} However, with the advent of Gamma Knife radiosurgery (GKRS), patients as well as neurosurgeons are often inclined to opt for GKRS instead of a second surgery for PMs. However, isolated TN requires more doses of GKRS than isolated meningioma of the posterior fossa. In addition, a neurosurgeon may wonder what to address while selecting the dose: to address the cause (tumor) or to address the effect (TN). We report our experience of management of recurrent PM with TN for patients who underwent two to five procedures, and we propose a guideline to manage them adequately.

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Materials and Methods

This study was performed after approval by the institutional review board at LSU Health (Shreveport, Louisiana, United States). Information related to clinical history, neuroimaging, microsurgical dissection, and outcomes of the patients with TN associated with PM between January 1995 and December 2014 was collected retrospectively by review of each patient's case notes, follow-up chart, and radiology reports. Patients with PM who were referred to our center for a primary complaint other than TN were excluded from this study (►Fig. 1). Over the past 20 years, 1,100 patients have been treated for meningioma, 57 patients experienced PM, and among them only six patients were found to have recurrent TN associated with PM in our institution.

Patients' Demographics

The median age of the patients in this study was 47 years (range: 21–66 years). Of the six patients, three(50%) were men and three (50%) were women. Most of the patients (83%) were white. ►Table 1 reports the details of the characteristics of TN.

Treatment Approaches

All of the patients in this study underwent microsurgical resection with microvascular decompression or gamma knife surgery as a primary or secondary treatment. Gamma knife stereotactic radiosurgery was performed using the Leksell stereotactic unit, model "C" with automatic positioning system (Atlanta, Georgia, United States). The Leksell Gamma Plan software, v.5.34, was used to perform the dose planning. The median radiation dose was 80 when GKRS was performed as primary treatment for TN. However, the median dose was 13 Gy for the treatment when GKRS was performed as treatment for meningioma with or without surgery. The treatment strategy is outlined in ►Table 2.

Assessment of Intensity of Pain

We have assessed the intensity of TN according to the Barrow Neurosurgical Institute (BNI) pain score; BNI score I: no trigeminal pain, no medication; BNI score II: occasional pain, not requiring medication; BNI score III: some pain, adequately controlled with medication; BNI score IV: some pain, not adequately controlled with medication; and BNI score V: severe pain, no pain relief.

Fig. 1 Exclusion criteria of selection of patients with petroclival meningioma associated with trigeminal neuralgia.

Table 1 Characteristics of patients with trigeminal neuralgia associated with petroclival meningioma

Variables	Value
Age, y	
Median	47
Range	21–66
Gender (%)	
Male	3 (50)
Female	3 (50)
Ethnicity (%)	
White	5 (83)
African American	1 (17)
Tumor location	
Petroclival	6
Distribution of trigeminal nerve pain	
V2	4
V2/V3	2
Tumor size before treatment, cm (range)	
GKRS	1.4 (0.8–2)
Resection	3.3 (3–4.1)
First intervention	
GKRS (%)	2 (33)
Prior resection (%)	4 (67)
Median follow-up, mo (range)	149 (62–236)

Abbreviation: GKRS, Gamma Knife radiosurgery.

Follow-up

Preoperative and follow-up data were collected from the study population. If necessary, patients were contacted by telephone to update their outcome status. Neuroimaging studies were done at 3-month intervals in the first year of the treatment, at 6-month intervals for the following 2 years, and annually thereafter. These detailed neurologic examinations identified improvement or worsening of preexisting symptoms, development of any new symptoms, and any change in magnetic resonance images. The median duration of follow-up was 149 months (range: 62–236 months).

Statistical Analysis

Commercially available software, SPSS v.21.0 (SPSS, Inc., Chicago, Illinois, United States), was used for statistical analysis. When necessary, a chi-square test and Student *t* test were used. A *p* value < 0.05 was considered significant.

Results

Control of Trigeminal Neuralgia

The pain-free period in resection group was 4 years after primary treatment. However, the pain-free period was 2 years in the GKRS group. This difference in pain-free

period between the two groups reached statistical significance (*p* = 0.034). In last follow-up, pain was controlled in four patients (67%). In the GKRS group, pain recurred in 50% of the patients,; but in the resection group, pain was controlled in 75% of the patients, and 25% of patients showed recurring pain. Both patients (100%) in the GKRS group required further resection to control the pain. In the resection group, 75% patients required repeat resection of the tumor to control the recurrent pain. One patient in the resection group was elderly and experienced other comorbidities, and therefore GKRS was preferred over repeat resection because of recurrent pain (► **Table 2**).

BNI Pain Score in This Series

In the present study, recent follow-up showed that TN was relieved in four patients. However, one patient in the resection group continued to experience severe pain in the maxillary and mandibular (V2/3) areas controlled with pregabalin. Similarly, the elderly patient treated with GKRS alone after three resections was experiencing mild TN in the mandibular (V3) area controlled with amitriptyline and carbamazepine (► **Table 3**).

Tumor Growth Control

Rate of tumor growth control after treatment is listed in ► **Table 3**. The average tumor size before GKRS was 1.4 cm and before resection was 3.3 cm. The most recent follow-up showed arrested tumor growth in one patient and increased tumor size in 5 patients (83%) after primary treatment (► **Fig. 2**).

Functional Status

We applied the Karnofsky performance score (KPS) in this case series and observed that there was significant difference in the KPS after treatment compared with pretreatment (78 versus 88). Three patients (50%) had an improved KPS scale, and three (50%) had no change in the KPS scale after treatment. Both patients in the GKRS group showed no improvement in KPS; however, of four patients in the resection group, three patients showed improvement in KPS (► **Table 4**).

Other Neurologic Findings

After treatment, the total number of symptoms was significantly improved when compared with the number of symptoms prior to treatment (pretreatment: 14 [233%] versus posttreatment: 4 [67%]). The visual problem was markedly improved after treatment (pretreatment: 2 [33.33%] versus posttreatment: 0 [0%]). Facial nerve dysfunction (16.6% versus 0%), hearing deficits (16.6% versus 0%), headache (50% versus 16.6%), and dizziness (16.6% versus 16.6%) were reduced after treatment, although there was no significant difference (► **Table 4**).

Discussion

TN is usually caused by hyperexcitability of the trigeminal nucleus following continuous irritation of the nerve in its entry zone by either an artery or vein.^{3,12–15} Among the

Table 2 Treatment strategy and outcome

Case	Primary treatment strategy	Subsequent treatment 1: dose, reason, and interval	Subsequent treatment 2: dose, reason, and interval	Subsequent treatment 3: dose, reason, and interval	Present status
1	Sx	GKRS, 13 Gy, small residual tumor, no significant pain; 13 mo	–	–	Pain relieved
2	Sx	Sx, recurrence of pain and tumor, 5 y	Sx and GKRS, 13 Gy; same sitting with third surgery for the minimal residue recurrence of pain and tumor, 11 y	GKRS alone, 12 Gy recurrence of pain, elderly patient with comorbidities 3.5 y	V2/3 pain controlled with medication
3	GKRS as primary treatment for TN; dose was high (80 Gy)	Sx, recurrence of pain and tumor, 2 y	–	–	V3 pain controlled with medication
4	Sx	Sx, recurrence of pain and tumor, 5 y	GKRS, small residue, 2 mo after Sx	–	Pain relieved
5	Sx	Sx, recurrence of pain, 3.5 y	GKRS, 13 Gy tumor, 1 mo after second Sx for the small residue	Sx, recurrence of pain and tumor, 8 y	Pain relieved
6	GKRS, as primary treatment for TN; dose 80 Gy	Sx, recurrence of pain and tumor, 2 y	–	–	Pain relieved
7	GKRS, small tumor, occasional TN; 13 Gy	–	–	–	Pain relieved

Abbreviations: GKRS, Gamma Knife radiosurgery; Sx, resection; TN, trigeminal neuralgia.

cranial tumors, vestibular schwannoma, epidermoid tumor, and meningiomas are mostly causing TN. The incidence of TN due to intracranial tumors is ~ 0.8% of all TNs.¹⁶ Posterior fossa meningioma including PM is more prone to cause TN than tumors in any other locations. Several large series have suggested that in these cases the trigeminal nerve is not only compressed by the vessel but also by the tumor itself.² Therefore, treatment of the patients with meningioma and

TN warrants careful examination to detect the presence of vascular compression and to decide whether they require a decompression of vessel along with resection of the tumor.²

In this series of six patients, four patients had suboccipital retromastoid microsurgical resection, and two patients had GKRS as an initial treatment. Of six patients who underwent initial treatment either with GKRS or resection, five patients experienced recurrent TN and required further intervention.

Table 3 Barrow Neurological Institute pain score at last follow-up

Case no.	Pre-BNI score	Complaints and medication posttreatment	Post- BNI score
1	IV	No TN pain; no medication	I
2	V	V2/3 pain; pregabalin	III
3	V	Occasional V3 pain; amitriptyline and carbamazepine	III
4	IV	No TN pain; no medication	I
5	V	No TN pain; no medication	I
6	IV	No TN pain; no medication	I
7	III	No TN pain; no medication	I

Abbreviations: BNI, Barrow Neurological Institute; TN, trigeminal neuralgia.

Fig. 2 (A) Preoperative gadolinium-enhanced magnetic resonance imaging (MRI) showing a right petroclival meningioma. (B) Postresection gadolinium-enhanced MRI at 2-year follow-up showing no recurrence of the tumors.

We preferred GKRS initially to treat the patients who had severe TN (BNI score IV/V) but smaller tumors (1.4 cm), and we performed maximal safe resection for larger tumors (3.3 cm) and severe pain (BNI score = IV/V). The patient's pain assessment and satisfaction survey at follow-up revealed that the pain-free period was 2 years for the GKRS group and 5 years for the resection group ($p = 0.034$), respectively.

In the resection group, pain was relieved for one patient after primary treatment but required GKRS for residual tumor. Two patients required further treatment with resection and upfront GKRS to relieve the pain. Another patient had resection and upfront GKRS, but this patient continued to have pain that was controlled with medication.

In the GKRS group, one patient required resection again to control pain, but another patient had persistent pain although

less than what he experienced prior to GKRS. Luckily the pain could be controlled with medication, obviating the need for a second procedure. Of the six patients with recurrence TN, four patients had BNI score I and two patients had BNI score III (some pain controlled with medication).

TN Associated with PM and Surgery

Surgical procedures are selected according to patients' age, comorbidities, prior mode of treatment, and last, but not least, the patient's preference. Resection is the primary and popular method of treatment for TN. It is a safe and effective method to resolve TN with preservation of trigeminal nerve function for most patients.^{3,17–20} The approaches of surgery

Table 4 Clinical outcome after treatment

Clinical features (%)	Pre-Rx	Post-Rx	<i>p</i> value
Trigeminal neuralgia	6 (100)	2 (33.3)	0.0001
Headache	3 (50)	1 (16.6)	NS
Visual impairment	2 (33.3)	0 (0)	NS
Facial nerve dysfunction	1 (16.6)	0 (0)	NS
Hearing deficit	1 (16.6)	0 (0)	NS
Dizziness	1 (16.6)	1 (16.6)	NS
Total symptoms, all patients (%)	14 (233)	4 (67)	0.0001
GKRS	3 (50)	1 (16.6)	0.0001
Resection	11 (157)	3 (50)	0.0001
KPS, all patients	78.33	88	0.044
GKRS	80	80	NS
Resection	77.5	92	0.02

Abbreviations: GKRS, Gamma Knife radiosurgery; KPS, Karnofsky performance score; NS, not significant; Rx, prescription.

also have some effects on the outcome of patients with TN-associated PM. Kuroki et al suggested that the anterior petrosal approach for petrous meningioma with TN is superior to the retrosigmoid approach for better visualization, control of bleeding, and less damage to the neurovascular structure.²

TN Associated with PM and Gamma Knife Radiosurgery
Radiosurgery is an emerging procedure to control trigeminal pain.^{19,20} However, although petroclival tumor can be controlled by GKRS, control of trigeminal pain is uncertain due to unclear data in the existing literature.² Additionally, it may take a longer time to achieve pain control with GKRS. Furthermore, the duration of pain control with GKRS is shorter and accompanied by radiosurgery-related neurologic deficits.²¹ Although there are no data on recurrent TN associated with PM, existing data in the literature suggest that resection with direct supervision of vascular compression is a better approach to control a primary tumor as well as TN.² Another issue of concern here is to choose the dose of GKRS. Although a dose of 14 Gy may be enough for a PM, it may not be sufficient to control the pain when they are associated with TN. Therefore addressing the TN should be preferred over targeting only the tumor.

Comparison of the Procedures (Surgery versus GKRS)

Literature review suggested that the pain-free rate with resection and GKRS treatment is 73.6% and 44%, respectively. In addition, although patient satisfaction was almost 100% immediate after both procedures, at follow-up

only 75% of patients in the GKRS group responded that they would have same procedure again or would recommend the procedure for their family or friends. However, 100% patients with TN expressed satisfaction with resection. Thus authors have concluded that resection is superior to GKRS as a treatment of TN.^{19,20,22,23}

Our Experiences and Summary

We had a patient with occasional (BNI score III) TN associated with small PM (2 cm) who was treated with GKRS as primary treatment. That patient did not experience a recurrence of TN. Thus GKRS as an initial treatment may be tried in patients with small PM, patients with comorbidities, and according to the patient preferences. However, from our experience, it is clear that patients with recurrent trigeminal pain after initial GKRS should be treated with resection rather than using GKRS again because radiosurgery does not result in prolonged pain relief. Moreover, patients treated with initial resection, repeated resection, or resection with upfront GKRS should receive further intervention because adjunct therapy with GKRS cannot control the pain for a long period. Subtotal resection of PM is performed sometimes due to its anatomical location, and upfront GKRS would be the better choice for these patients. Therefore, resection has an overall better outcome than GKRS alone in controlling recurrent trigeminal pain associated with PM (→Fig. 3). However, the complications of surgery including the neurovascular injury, cerebrospinal fluid leakage, wound infection, hearing loss, pneumonia, and deep vein thrombosis should be considered. Further study with a large volume of patients is warranted to better understand

Fig. 3 Summary of the treatment approach for petroclival meningioma associated with trigeminal neuralgia. GKRS, Gamma Knife radiosurgery.

the effectiveness of resection compared with other treatment procedures in patients with recurrent TN associated with PM.

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