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Original Article

Gamma knife radiosurgery for cerebellopontine angle epidermoid tumors

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Abstract

Background: Intracranial epidermoid tumors are commonly found in the cerebellopontine angle where they usually present with either trigeminal neuralgia or hemifacial spasm. Radiosurgery for these tumors has rarely been reported. The purpose of this study is to assess the safety and clinical outcome of the treatment of cerebellopontine epidermoid tumors with gamma knife radiosurgery.

Methods: This is a retrospective study involving 12 patients harboring cerebellopontine angle epidermoid tumors who underwent 15 sessions of gamma knife radiosurgery. Trigeminal pain was present in 8 patients and hemifacial spasm in 3 patients. All cases with trigeminal pain were receiving medication and still uncontrolled. One patient with hemifacial spasm was medically controlled before gamma knife and the other two were not. Two patients had undergone surgical resection prior to gamma knife treatment. The median prescription dose was 11 Gy (10–11 Gy). The tumor volumes ranged from 3.7 to 23.9 cc (median 10.5 cc).

Results: The median radiological follow up was 2 years (1–5 years). All tumors were controlled and one tumor shrank. The median clinical follow-up was 5 years. The trigeminal pain improved or disappeared in 5 patients, and of these, 4 cases stopped their medication and one decreased it. The hemifacial spasm resolved in 2 patients who were able to stop their medication. Facial palsy developed in 1 patient and improved with conservative treatment. Transient diplopia was also reported in 2 cases.

Conclusion: Gamma knife radiosurgery provides good clinical control for cerebellopontine angle epidermoid tumors.

Key Words: Cerebellopontine, epidermoid, gamma knife, radiosurgery

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INTRODUCTION

Intracranial epidermoid tumors are commonly found in the cerebellopontine angle,[18,32,43] with 40% occurring in this location.[22] They commonly present with hyperactive cranial nerve dysfunction, namely trigeminal neuralgia and hemifacial spasm.[44] It is believed that irritant chemical agents contained in the epidermoid tumor might cause toxic effects on the nerve root with disintegration of the myelin sheaths.[23,40] Although surgery is the mainstay of treatment and potentially curative, there are portions of the tumor capsule that are densely adherent to critical neurovascular structures making its removal without resulting in morbidity a challenging task. The capsule of epidermoid tumors is composed of keratinizing stratified squamous epithelium, which is similar to the squamous epithelium found in craniopharyngiomas. Because radiosurgery has been successfully used in craniopharyngiomas, the same can be expected with epidermoid tumors. Inducing cell death in the tumor capsule would result in reduction of debris accumulation inside these tumors stopping growth.

Recently, radiosurgery has emerged as a treatment option for cerebellopontine epidermoid tumors. Very few have reported on the radiosurgical treatment of these tumors. The purpose of this study was to assess the safety and clinical outcome of the treatment of cerebellopontine epidermoid tumors with gamma knife radiosurgery.

PATIENTS AND METHODS

This is a retrospective study involving 12 patients harboring cerebellopontine angle epidermoid tumors that were treated between May 2008 and November 2013. A single session was conducted in 9 patients. Volume-staged radiosurgery was done in 3 patients due to large tumor size; it was a two-staged treatment in these 3 patients. The interval between the treatment stages was 3 months.

The Leksell stereotactic head frame was attached to the patient's head using local anesthesia (model G, Elekta AB). Imaging was based on contrast-enhanced T1-weighted sequences plus T2-weighted magnetic resonance (MR) sequences with 1.6-mm slice thickness using high-resolution 1.5-T magnetic resonance imaging (MRI) (Genesis Sigma, General Electric). Stereotactic images were imported into the GammaPlan workstation (Elekta AB). The treatment was carried out using the Gamma Knife Model C and Gamma Knife PERFEXION (Elekta Instruments, Inc.). The target volume was drawn in all the MRI slices. We selected a prescription dose of 11 Gy or less to keep the dose to the adjacent brainstem below the 12 Gy toxicity threshold.

The median prescription dose was 11 Gy (10–11 Gy). The tumor volumes ranged from 3.7 to 23.9 cc (median 10.5 cc). The median treated target volume (i.e., the target volume/treatment) was 7.6 cc, taking in consideration the target volumes in the staged treatment cases [Table 1]. The median radiological follow-up was 2 years (range 1–5 years). The median clinical follow-up was 5 years (range 1–7 years) performed via communications with the patients' treating physicians.

Imaging follow-up examinations using contrast-enhanced MRI were carried out at 6-monthly intervals for the first 2 years and then annually thereafter. Additional imaging was obtained when a patient developed new symptoms or experienced worsening of any preexisting symptoms.

Every patient's history and clinical examination findings were recorded and compared with those documented prior to treatment. Radiological follow-up was undertaken by performing contrast-enhanced MRI. In addition to imaging,

Table 1: Treatment parameters

Patient no.	Treated target volume (cc)	Prescription dose (Gy)	Prescription isodose (%)	No. of shots	Collimator sizes (mm)	Conformity index
1	23.9	10	50	20	8, 14	1.17
2	6.8	11	50	14	8, 14	1.22
3	22	11	50	15	14, 18	1.44
4	9.7	11	50	13	8, 14	1.37
5	7.1	11	50	12	8, 14	1.58
6	9.7	11	50	14	14	1.6
7	7, 8.5§	11, 11	50, 50	11, 12	(14) - (14, 18)	1.32, 1.5
8	11.3	11	50	11	18	1.56
9	6.8	11	50	9	14	1.63
10	7, 10.7§	11, 11	60, 50	11, 32	(14) - (4, 8, 16)	1.64, 1.28
11	7.6, 5.7§	11, 11	50	27, 20	(B, 4, 8) - (4, 8, 16)	1.27, 1.3
12	3.7	11	50	26	4, 8, 16	1.4

Patients no. 1 to 9 and 10 (first stage) were treated with Gamma Knife Model C. Patients no. 10 (second stage), 11 and 12 were treated with Gamma Knife Perfexion. B Blocked collimator. §Volume-staged gamma knife treatment

an audiometry with speech discrimination score was performed at every follow-up to assess the hearing status due to the presence of the hearing apparatus (cochlear nerve and cochlea) in the tumor vicinity.

The trigeminal pain after gamma knife treatment at the last clinical follow-up was assessed and classified according to the Barrow Neurosurgical Institute (BNI) score.[30] After gamma knife treatment the trigeminal pain with BNI scores I, II, and IIIa were considered as "controlled," IIIb was considered as "partially controlled," and IV and V were considered as "uncontrolled."

RESULTS

Patient demographics

The patients were 23–50 years (median 35 years) of age. There were 9 males and 3 females. Two patients underwent previous surgery. One had been operated twice and recurred for the third time (the first time after 2 years and the second after 3 years). The other had a residual tumor after surgery. The remaining 10 patients were diagnosed based on MRI radiological features. Hyperactive cranial nerve dysfunction (trigeminal neuralgia or hemifacial spasm) was present in 9 patients (9/12, 75%). This was in the form of trigeminal pain in 8 patients (8/12, 67%) and hemifacial spasm in 3 patients (3/12, 25%). Among these 9 patients, 2 had combined trigeminal pain and hemifacial spam (2/12, 17%) and 1 patient had hemifacial spasm only (1/12, 8%). All cases with trigeminal pain were receiving medication and still uncontrolled. One patient with hemifacial spasm was medically controlled before gamma knife and the other two were not [Table 2].

Treatment outcome [Table 3]

Hyperactive cranial nerve dysfunction improved or resolved in 5 out of 9 patients (56%). The trigeminal pain was controlled in 5 out of 8 (63%) patients, and of these, 4 cases stopped their medication and 1 decreased it. The hemifacial spasm resolved in 2 of 3 (67%) patients who were able to stop their medication. The two patients who had combined trigeminal pain and hemifacial spasm showed resolution of their symptoms and were able to stop all medication. The median time to pain improvement was 9 months (6–14 months).

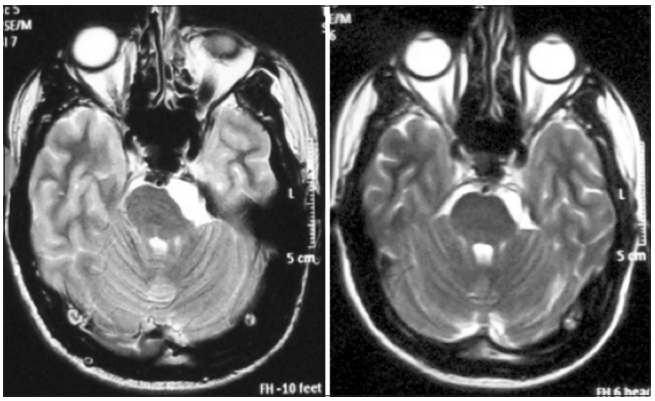

Figure 1: A 28-year-old male presented with left V2, V3 trigeminal neuralgia (BNI IV) for 2 years which had become unresponsive to medication. MRI T2-weighted image (left) showed he had a left cerebellopontine angle epidermoid 6.8 cc in volume. The tumor was treated with 11 Gy to the 50% isodose. At 6-month follow-up, the tumor shrank and the patient's trigeminal pain improved (BNI IIIa) and he was able to decrease his medication. One year later, however, his trigeminal pain had recurred (BNI IIIb). At 5 years, the tumor was still under control (right)

Table 2: Patient demographics

Patient no.	Sex	Age	Previous surgery (no. of surgeries)	Clinical presentation	Medical control (TN/HFS)	Duration of TN/HFS (months)
1	M	38		Diminished hearing	NA	NA
2	M	28		Trigeminal pain	No	24
3	M	47	Tumor resection (2)-recurrence	Trigeminal pain Facial numbness Diminished hearing	No	36
4	M	23		Meningism Ataxia	NA	NA
5	F	27	Tumor resection (1)-residual	Trigeminal pain	No	36
6	F	27		Hemifacial spasm	Yes	4
7	M	29		Diplopia (Abducent nerve palsy)	NA	NA
8	M	46	Neurectomies for facial pain (6)	Trigeminal pain	No	96
9	M	39		Trigeminal pain Hemifacial spasm	No	12
10	F	28		Trigeminal pain Hemifacial spasm	No	3
11	M	33		Trigeminal pain	No	12
12	M	50		Trigeminal pain	No	8

TN: Trigeminal neuralgia, HFS: Hemifacial spasm, NA: Not applicable (no trigeminal pain before gamma knife treatment)

Table 3: Clinical and radiological treatment outcome

Patient no.	Clinical presentation	BNI score after gamma knife	Time to pain improvement (months)	Hearing outcome	Clinical follow-up duration (years)	Radiological outcome	Radiological follow-up duration (years)	Complications (Timing)
1	Diminished hearing (non-serviceable)	NA	NA	Non-serviceable (same)	1.3	Stable	1.3	
2	Trigeminal pain	IIIb	PC	Serviceable	7.3	Shrank	5.4	
3	Trigeminal pain Facial numbness Diminished hearing	IV	UC	Serviceable	6.7	Stable	1.3	
4	Meningism Ataxia	NA	NA	Serviceable	6.6	Stable	1.0	
5	Trigeminal pain	II (C)	6	Serviceable	6.4	Stable	1.1	
6	Hemifacial spasm	NA	NA		5.9	Stable	2.0	
7	Diplopia (Abducent nerve palsy)	NA	NA	Non-serviceable (worse)	5.2	Stable	1.3	Transient facial palsy (after 9 months)
8	Trigeminal pain	IV	UC	Serviceable	5.1	Stable	4.6	
9	Trigeminal pain Hemifacial spasm	I (C)	14	Serviceable	3.7	Stable	3.1	Transient diplopia (after 37 months)
10	Trigeminal pain Hemifacial spasm	I (C)	11	Serviceable	3.7	Stable	3.6	
11	Trigeminal pain	IIIa (C)	9	Serviceable	2.8	Stable	1.9	Transient diplopia (after 10 months)
12	Trigeminal pain	I (C)	8	Serviceable	1.5	Stable	1.5	

NA: Not applicable (no trigeminal pain before gamma knife treatment), C: Controlled trigeminal pain (BNI I, II, IIIa), PC: Partially controlled trigeminal pain (BNI IIIb), UC: Uncontrolled trigeminal pain (BNI IV and V)

Trigeminal pain was partially controlled in 1 patient and was uncontrolled in 2 patients. The duration of symptoms before treatment was 2–8 years. The first patient had initial pain improvement at 6 months which recurred at 1 year (BNI IIIb) [Figure 1]. The other 2 patients did not experience any improvement in their pain after treatment. One patient was initially a tumor recurrence after two previous operations at the time of gamma knife treatment. He underwent reoperation 4 years after gamma knife treatment because of unresolved trigeminal pain. His facial pain improved after surgery but he developed bothersome facial numbness. The other patient had undergone six neurectomies before treatment.

Hemifacial spasm was uncontrolled in 1 patient. He presented 4 months after onset of his symptoms. There was initial improvement of spasm at 6 months and was even able to stop his medication. The hemifacial spasm recurred at 18 months.

Ten patients had serviceable hearing before treatment. All 10 patients retained serviceable hearing after treatment. One patient who had nonserviceable hearing before treatment developed further worsening of his hearing and eventually became deaf at 2-year follow-up. This was a patient who had a large tumor that was treated by volume-staging. All tumors were radiologically controlled. One tumor shrank and the others remained stable.

Complications

One patient developed transient facial nerve palsy (House-Brackmann Grade 3) at 8 months after treatment. It improved with conservative treatment to Grade 2 approximately 6 months later. Transient diplopia developed in 2 patients 10 and 37 months after treatment.

DISCUSSION

Epidermoid tumors are typically benign lesions that commonly occur in cerebellopontine angle. They usually present with hyperactive cranial nerve dysfunction, mainly trigeminal neuralgia and hemifacial spasm. The incidence of trigeminal neuralgia in patients with cerebellopontine epidermoid tumors is reported to vary from 0 to 77%,[6,7,12,14,18,21,25,33,35,39,42] whereas the incidence of hemifacial spasm ranges from 0 to 13%.[5,18,22,23,36,43] A combination of ipsilateral trigeminal neuralgia and hemifacial spasm has also been reported.[10,16,26] The incidences of trigeminal neuralgia and hemifacial spasm in the current study were within the reported ranges [8/12 (67%) and 1/12 (8%), respectively]. We also had 2 patients with combined trigeminal neuralgia and hemifacial spasm.

Surgery

Surgery remains the primary treatment option of cerebellopontine angle epidermoid tumors. The controversy has been whether to proceed with radical tumor resection or subtotal/near total resection. Radical resection should involve removal of the tumor capsule that has tumor cells, which desquamate giving rise to the cyst contents.[37] Obviously, total removal is the ideal option as

it is thought to reduce recurrence but it may be associated with an increased incidence of morbidity. This is because there are portions of the tumor capsule that are adherent to the adjacent neurovascular structures making complete tumor removal extremely difficult without significant complications and morbidity.[3,8,12,20,35,36,43] Moreover, the capsule is often translucent and difficult to distinguish from the arachnoid of the posterior fossa.[37] On the other hand, subtotal removal may yield better surgical outcome but is thought to be associated with higher rates of recurrence. Consequently, some authors have promoted radical tumor resection to prevent recurrence,[3,43] whereas others have advocated a more conservative approach to minimize operative morbidity and mortality.[8,20,36,42,45] Other authors have doubted that the degree of tumor resection contributed to the risk of recurrence.[2,37]

Previous studies have reported recurrence of epidermoid tumors to occur from 1 year to several years after surgery in up to 26% of the cases, even with complete tumor removal.[3,4,11,18,37] Some authors have suggested reasons for early recurrence such as accelerated proliferation induced by spillage of cyst contents,[31] carcinomatous transformation,[1,9,13,19,24,28] or a large number of residual clonal cells.[27] In the current series we had one case of tumor recurrence after surgery that had undergone surgery twice and both times there was no histopathological or radiological evidence of malignancy, yet recurrence was observed after 2 then 3 years. The fact that these tumors recur suggests that at least some epidermoid tumors are actively growing and will progress over time if left untreated.

Gamma Knife results

Gamma knife radiosurgery for cerebellopontine angle epidermoid tumors has rarely been reported. Kida *et al.*[17] reported on 7 cases and Vasquez *et al.*[41] reported on 3 cases. To our knowledge, the current study is the largest case series to report on radiosurgery for cerebellopontine angle epidermoid tumors.

Previous gamma knife reports have indicated complete trigeminal pain or hemifacial spasm relief or improvement in all treated cases.[17,41] Although the current study had a similar follow-up period as the other reports of 57 months, our results were inferior regarding clinical outcome. This may be explained by the lower prescription doses and larger tumor volumes given in the current series, as larger tumors are expected to cause more nerve compression as well as irritation to a greater length of cranial nerve; hence, the hyperactive nerve dysfunction in these cases would be more resistant to treatment. Furthermore, two cases that did not show any improvement were already resistant to treatment before gamma knife, with one case having had two previous surgeries and one case had undergone several neurectomies. Moreover, Vasquez *et al.*, in two of their patients, gave an additional booster dose to the trigeminal nerve.[41] The explanation for clinical improvement was suggested to be because of nerve radiosurgical decompression.[17] Another possible reason may be neuromodulatory effect of radiation on the nerve.[29]

Radiological tumor control was reported in all cases in the current series as with other series in all cases.[17,41] Kida *et al.* even reported tumor shrinkage in two cases.[17] Similarly, we observed tumor shrinkage in one case, yet the majority of cases showed unchanged tumor size. It would make more sense for tumor size to remain unchanged after gamma knife treatment because the cyst content is non-living debris with keratin and cholesterol. The possible explanation for tumor shrinkage in these cases would be cyst leakage and minor content spillage.

Complications

Kida *et al.* reported 1 patient who developed permanent diplopia and another who had hearing loss after gamma knife treatment. In the current study, we had two cases of transient diplopia and one case of hearing loss. We reported one case of facial nerve palsy after treatment, which was not observed in any of the previous series. In this case, it was a transient occurrence and facial nerve function eventually improved. This was unusual because of the lower dose used compared to the other studies. There is the possibility that the patient had undergone volume-staged treatment so the facial nerve supposedly received radiation twice. Yet, no facial nerve dysfunction was observed in the other two volume-staged cases. In our opinion, it may be related to individual patient radiosensitivity, the length of facial nerve irradiated in the cerebellopontine angle, or the position of the hotspot inside the tumor.

Surgical series have reported the incidence of postoperative facial nerve palsy to be up to 20%,[15,18,38] and the incidence of postoperative ocular nerve palsy to be up to 20% also.[11,15,18,34,38] The incidence of transient facial nerve palsy (one case) and ocular nerve palsy (two cases) in the current study was 8 and 17%, respectively, which was not significantly different from surgery. Yet, surgery carries other risks not present with gamma knife treatment such as bulbar palsy, ataxia, motor weakness, cerebrospinal fluid leak, and meningitis [Table 4]. Moreover, hearing deterioration was reported to occur in up to 27% of surgical series yet only reported in one case in the current series.

Study limitations

The main limitation of this study is the relatively short radiological follow-up compared to similar studies. The short follow-up does not allow differentiation from natural history. However, we could clinically follow-up all the patients by phone for a relatively long-term period to establish clinical efficacy.

Although surgery remains the gold standard for the treatment of cerebellopontine angle epidermoid tumors, we suggest gamma knife may have a role in small

Table 4: Recent cerebellopontine angle epidermoid surgical series in literature

Surgical series	Total no. of patients	Total tumor removal (%)	Tumor recurrence (%)	New postoperative cranial nerve deficit						Postoperative complications				Hyperactive nerve dysfunction outcome		Mean follow-up (yrs)
				III and IV (%)	V (%)	VI (%)	VII (%)	VIII (%)	Lower Cr. n (%)	Meningitis	CSF leak	Other*	%	TN improvement (%)	HFS improvement (%)	
Kobata, 2002[18]	30	17 (57)	2 (7)	3 (10)	18 (60)	6 (20)	6 (20)	8 (27)	3 (10)	3	1	4	27	28/28 (100)	2/2 (100)	11.5
Schroeder, 2004[38]	8	8 (100	0	0	1 (13)	1 (13)	1 (13)	1 (13)	0	0	0	0	0	NA	NA	3.8
Safavi-Abbasi, 2008[34]	12	9 (75)	0	0	0	0	1 (8)	0	1 (8)	0	1	1	17	2/3 (67)	2/4 (50)	2
Schiefer, 2008[37]	24	13 (54)	6 (25)	0	0	0	0	2 (8)	0	2	1	1	17	5/10 (50)	0	4.2
Gopala krishnan, 2014[11]	50	11 (22)	13 (26)	0	0	0	2 (4)	0	2 (4)	1	2	1	8	10/13 (77)	3/4 (75)	9.4
Hasegawa, 2015[15]	22	18 (82)	0	0	0	1 (5)	1 (5)	0	2 (9)	0	0	4	18	11/13 (85)	5/6 (83)	2

*Hydrocephalus, hemiparesis, ataxia, nystagmus, TN: Trigeminal Neuralgia, HFS: Hemifacial Spasm, NA: No available data

symptomatic tumors, residual tumors, or as an alternative when surgery cannot be performed.

CONCLUSION

Gamma knife radiosurgery provides long-term symptomatic relief for the hyperactive nerve dysfunction associated with these tumors. The minimal and acceptable complications make gamma knife radiosurgery a safe treatment option for cerebellopontine angle epidermoid tumors. Future prospective long-term studies should be conducted, preferably with controls, to further substantiate the efficacy.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Nil.

Conflicts of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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