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Gamma knife radiosurgery of epidermoid tumors: an analysis of treatment results of eight patients

Ryan L. Hellinger, Aizik L. Wolf, Beatriz Amendola, Sammie Coy

Innovative Cancer Institute, South Miami, Florida, United States
Miami Neuroscience Center, South Miami, Florida, United States

ABSTRACT

Background: Epidermoid tumors (ETs) of the central nervous system (CNS) are rare tumors that typically occur in the 4th decade. They typically grow around vital neurovascular structures which makes surgical treatment difficult. The objective of this paper is to report on the effectiveness and safety in the management of epidermoid tumors with gamma knife surgery (GKS).

Materials and methods: This is a retrospective study of the medical records of 8 patients treated with GKS for epidermoid tumors between July 2010 to June 2019. The median prescription dose was 11 Gy, ranging from 10 to 12 Gy, 5 patients received the total dose target to the 50% line and 3 to the 55% isodose line. The mean tumor volume was 12.4 cc ranging from 4.4 to 24.8cc. The median follow-up time was 33.7 months and ranged from 0.9 to 58.8 months. At follow-up, patients were evaluated for neurological signs and symptoms and radiographic evidence of progression of disease. Two patients were treated after failure of linac stereotactic radiosurgery. One patient underwent stereotactic radiosurgery prior to GKS, and the other had failed surgical resection prior to GKS.

Results: The median age was 33 years old. There were two males and six females. The most common presenting manifestation was headaches followed by vision and hearing problems. Symptoms were resolved in all cases, except for one who had partial control of trigeminal neuralgia. All patients were locally controlled by imaging and neurological examination at first follow-up.

Conclusion: Gamma knife surgery is a safe and effective alternative treatment in patients with CNS epidermoid tumors and should be included in the initial recommendation.

Key words: epidermoid tumor; radiosurgery; brain tumor; radiation therapy; surgery

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Introduction

Epidermoid tumors (ETs) are benign rare, slow-growing lesions that account for roughly 0.2 to 1.8% of all intracranial tumors [1]. They have been described as "pearly" and "the most beautiful tumors in the body" [2]. This pearly appearance comes from their keratin and fatty acid contents and stratified epithelium lining [3]. It is believed they derive from the neural tube entrapping ectodermal cells during closure between the 3rd and 5th weeks of embryonic development [4]. They are most commonly located in the cerebellopontine angle (CPA), accounting for 40% of epidermoid tumor cases and tend to accumulate around vital neurovascular structures causing trigeminal neuralgia and hemifacial spasms to be common symptoms [1, 5].

Total resection is a common neurosurgical recommendation of these tumors; nonetheless, it is difficult to do so while preserving the neurovascu-

Address for correspondence: Beatriz Amendola, Innovative Cancer Institute, South Miami, FL 33143, United States; e-mail: bamendola@innovativecancer.com

lar structures it surrounds [2]. This makes partial resection necessary to preserve neurological function. However, partial removal of these tumors typically leads to recurrence and thus reoperation [3]. GKS may be the preferred alternative therapy. There have been very few studies reporting on the treatment of epidermoid tumors with GKS [4-6]. This study aims to offer insight into the effectiveness and safety of treating epidermoid tumors with gamma knife surgery, compared to surgical intervention, and provide distinct reasons why this may be a favored treatment option.

Materials and methods

This is a retrospective study of eight patients (two males and six females, ages ranging from 22 to 56 with a median age of 33) who were treated with GKS for epidermoid tumors from July 2010 to June 2018 at the Miami Neuroscience Center. One patient received a craniotomy, and another received stereotactic radiosurgery before GKS while the other six have only undergone GKS. Patients were diagnosed preoperatively with computed tomography (CT) scans and magnetic resonance imaging (MRI) of the brain. Presenting symptoms were recorded at the initial visit.

The Leksell Gamma Knife stereotactic frame was placed on each patient's head using lidocaine as local anesthesia after appropriate premedication with 1 g of cefazolin and 20 mg of dexamethasone and intravenous sedation with propofol and midazolam. Imaging was based on MRI stereotactic localization of the lesion, visualization and volume dosimetry mapping. Radiosurgical treatment planning was done in conjugation with the radiation oncologist and the radiation physicist using gamma plan. The treatment plan consisted of an average of 22.4 isocenter. Treatment was carried out using the Perfexion Gamma Knife with a mean treatment time of 122 minutes (ranging from 48 minutes to 191 minutes). The median prescription dose was 11 Gy, ranging from 10 to 12 Gy, and five patients received the total dose target to the 50% and three to the 55% isodose line. The mean tumor volume was 12.4 cc ranging from 4.4 to 24.8cc.

The median clinical follow-up time was 33.7 months and ranged from 0.9 to 58.8 months. Patients follow-ups occurred in-person, except for one patient that followed up over the phone, and consisted of brain surveillance MRI imaging and clinical neurological evaluation after 1 month then in 3-months and then every 6 months or if there were new or worsening symptoms. At follow-ups, patients were evaluated for neurological and radiological progression of the disease.Clinical status was assessed by a complete neurological exam and patient history while radiographic status was determined by measuring tumor volume in cubic centimeters via MRI imaging. Neurological and radiographic progression was then determined to be stable, improved or worsened based on the change in pretreatment to post-treatment status. Radiographic progression was defined as an increase in tumor volume and tumor control was defined as unchanged or decreased tumor volume. Symptom control was defined as stable or improved symptoms.

Results

The median age was 33 years old with two males and six females. Follow-up growth was recorded for all patients except one due to being lost to follow up. The most common tumor location was the cerebellopontine angle (6/8), with one extending from the prepontine cistern to the interpeduncular fossa and another extending to the left prepontine cistern (Tab. 1). There was one temporal fossa lesion and one posterior fossa lesion that extended from the foramen magnum to the prepontine cistern. Most of the lesions were on the left side (5/8; Tab. 1). Six patients presented headaches, making it the most common symptom (Fig. 1). Three patients presented vision difficulties (loss, diplopia, vision changes) and three patients presented hearing difficulties, including hearing loss and tinnitus. Two patients presented trigeminal neuralgia. while four patients experienced pain in other parts of their body, including the neck, back, and shoulder (Tab. 1). Some patients used medicine (paracetamol or ibuprofen) to relieve their pain but with only partial control. Accompanying symptoms included nausea, dizziness, lack of balance, fatigue, and tingling sensation in the face and head in five patients.

None of the patients developed side-effects after GKS. Of the six patients presenting with headaches, none reported headaches one month after the procedure. Three of the six developed recurrent headaches, one for seven months with partial local control, and the other 2 at 31 and 16 months until headaches were fully resolved.

Table 1. Patients' backgrounds

Pt.	Age at treatment	Sex	Surgical history	Location	Symptoms	Total volume [cc]	Dose [Gy]
1	39	F	Craniotomy	Right temporal fossa	Headaches, blurred vision, nausea	7.8	12
2	52	F	Cyst removal of left breast	Left CPA extending to the left prepontine cistern	Headaches, tinnitus, vision changes, dizziness	24.8	11
3	22	F	Radiosurgery	Left CPA	Tinnitus, balance issues, tingling in face	13.7	10
4	25	F		Left CPA	Headaches, hearing loss, fatigue	14.7	11
5	28	M		Left CPA	Headaches	13.7	12
6	22	F		Posterior fossa cistern extending from foramen magnum to prepontine cistern	Headaches	9.4	11
7	38	M		Right CPA extending from prepontine cistern to the interpeduncular fossa	Trigeminal neuralgia, double vision, vision loss	11	11
8	56	F	Microdiscectomy	Left CPA	Headaches, trigeminal neuralgia	4.4	11

CPA — cerebellopontine angle

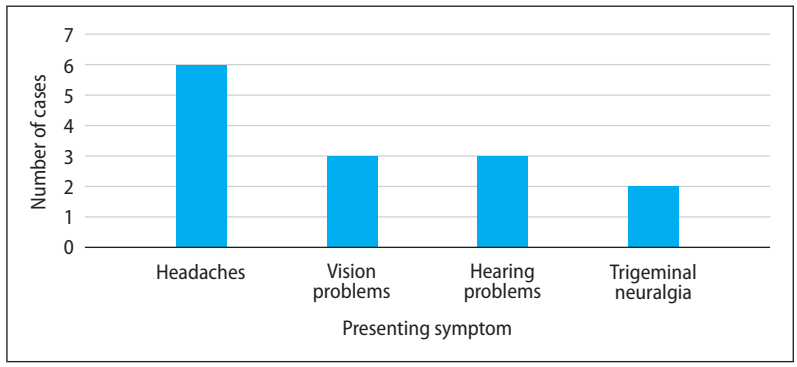

Figure 1. The most common presenting symptoms

One of the patients that presented with trigeminal neuralgia was only partially controlled 49 months after GKS. Another had recurring trigeminal neuralgia post GKS and was partially controlled by medications (carbamazepine), requiring a second GKS to the trigeminal nerve that resolved it after 18 months. Vision problems were resolved with all patients within one-month post GKS. Hearing problems were resolved in all cases. In one case, vision was resolved within a month and for the other two cases, the follow-up time was not recorded. All patients had tumor control or shrinkage (Tab. 2). One patient, in particular, experienced great reduction in tumor size, post GKS (Fig. 2). All accompanying symptoms were resolved in all patients.

Discussion

ET are benign unusual tumors that respond well and relatively fast to radiosurgery. In this retrospective study, GKS locally controls ET in all our cases with a median follow-up of 3 months.

Our results are consistent with data of prior ET GKS studies, including Vasquez et al., El-Shehaby et al., and Kida et al., with three, 12, and seven patients, respectively [4, 6]. These studies observed patients as asymptomatic until about the fourth decade, consistent with our study showing an average age at the treatment of 35 years. Common symptoms have been reported to be headaches, trigeminal neuralgia, vision and hearing difficulties

Table 2. Treatment outcomes

Patient	Presenting symptoms	Growth	Follow up (months)
1	Headaches, blurred vision	No	0.9
2	Headaches, tinnitus, vision changes	No	27.3
3	Tinnitus, balance issues, tingling in face	No	52.4
4	Headaches, hearing loss	No	11.8
5	Headaches	No	31.2
6	Headaches	No	58.8
7	Trigeminal neuralgia, vision problems	No	36.1
8	Headaches, trigeminal neuralgia	No	38.9

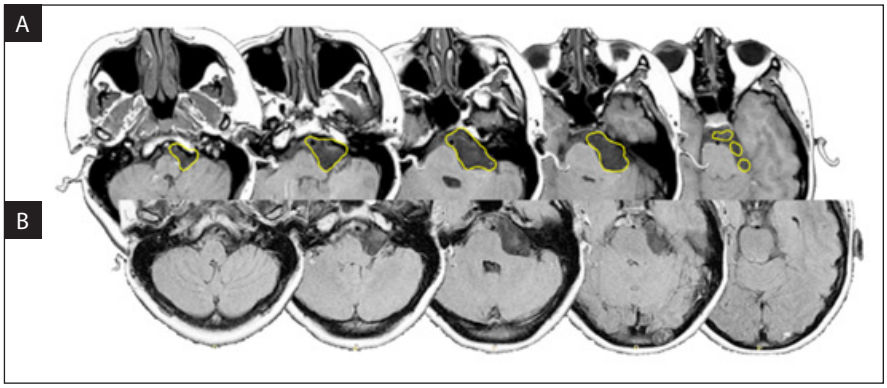

Figure 2. A. Pre-Gamma Knife MRI of patient 3 with a 13.7cc epidermoid tumor treated with 10Gy; **B**. Post-Gamma Knife MRI of patient 3 52.4 months showing tumor shrinkage

and seizures [4-5,7]. Unlike these other studies, our study does not have many patients reporting trigeminal neuralgia (2/8) or seizures (0/8).

Vasquez et al., El-Shehaby et al., and Kida et al. used a median prescription dose of 12 Gy, 11 Gy, and mean of 14.6 Gy respectively. These studies reported complete relief or improvement in almost all patients. Except for El-Shehaby et al., who reported trigeminal pain uncontrolled in two patients and partially controlled in one [5]. Similarly, our study had one of the trigeminal patients with partially controlled pain. Furthermore, all studies reported tumor control in all cases. These other studies reported a similar average follow-up time of 10, 38, and 53 months, respectively, compared to our 33.14 months [4–6].

Many have published on the success of surgical resection of ETs, including Lynch et al., De Souza et al., Kato et al. and Chowdhury et al.; however, there is a debate on the best approach (Tab. 3) [2, 7–9]. Many studies argue total removal is the best approach because it is believed to prevent recur-

Table 3. Data from epidermoid tumor (ET) surgical intervention studies

Author	Year of publication	Number of cases	Mortality (%)	Morbidity (%)	GTR (%)	Recurrence (%)	Follow-up (months)
Lynch et al.	2014	33	0	42.42	72.7	9	86.4
De Souza et al.	1989	30	3.7	40	18	14.8	108
Kato et al.	2013	27	5	33.33	10	20	N/A
Chowdhury et al.	2013	23	4.3	13.04	73.9	N/A	36
Overall		113	3.25	32.29	43.65	14.6	76.8

GTR — gross tumor removal; N/A — non available

rence [2, 7, 9]. However, difficulties arise due to Ets' proximity to the nerves and vascular structures [1, 2]. Partial removal appears to be a better option, but this could lead to recurrence. Therefore, GKS may be a more effective treatment.

While comparing cases of GKS and surgical treatment, GKS appears to be a better alternative when total removal does not seem possible or if there is a recurrence. GKS is a better alternative because it leads to a quicker recovery. The surgical treatment cases had an average follow-up time of 76.8 months (Tab. 3), while in the GKS studies, the average follow-up time was 33.53 months [2, 4–9]. GKS also has less recurrence, with only two out of the 30 cases (6.67%) of the previously mentioned GKS studies and this one included, showing recurrent symptoms or tumor growth. While the surgical studies have a recurrence of 14.6%. Furthermore, these studies report much higher morbidity of 32.29%, while the previously mentioned GKS studies report lower morbidity (13.33%) [2, 4–9].

Surgical removal could lead to permanent neurological deficits considering Ets' proximity to and encasement of vital structures, thereby making GKS a safer option [1, 2]. Other papers report a low mortality rate of surgical intervention of ETs, but GKS still leads to lower mortality. In the previously mentioned studies, surgical intervention has a mortality rate of 3.25% compared to GKS having a mortality rate of 0% (Tab. 3). We hope that this data encourages patients to look at GKS as an option when surgery is not preferred or there is recurrent tumor growth.

There are limitations in this case series due to its retrospective nature and relatively small sample size. We recognize it is difficult to make recommendations for clinical practice due to the lack of a reference group. Prospective studies comparing GKS to another treatment method should be employed to make a more definitive recommendation on the use of GKRS but would be unlikely due to the low incidence of glomus jugulare tumors.

Conclusion

This data confirms that GKS is an effective treatment for ET and a viable alternative to surgical intervention. GKS can be offered as an upfront alternative treatment of ET in unresectable patients or patients with high surgical risk as local control is maintained and the morbidity remains low or nil. Although the numbers of this series is small and the follow-up is short, the results are encouraging. Further follow-up is needed.

Conflict of interest

None declared.

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