Effectiveness and safety of Gamma Knife radiosurgery for glossopharyngeal neuralgia

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Glossopharyngeal neuralgia (GPN) is a rare disorder of the ninth cranial nerve characterized by severe paroxysmal pain affecting the ear, tongue, and throat. GPN can be associated with life-threatening issues such as cardiac arrhythmias, syncope, or malnutrition and weight loss from odynophagia. Though traditional treatment for GPN involves medical management at first and surgery for refractory cases, these therapies are often poorly tolerated in the elderly population. We describe the case of a 99-year-old woman, the oldest reported patient with GPN treated successfully with Gamma Knife radiosurgery. We conclude that Gamma Knife radiosurgery for GPN can be both effective and very well tolerated in the elderly and deserves further study and careful consideration as a treatment option in this population.

Glossopharyngeal neuralgia (GPN) is a rare disorder of the ninth cranial nerve characterized by severe, paroxysmal episodes of pain localized to the posterior tongue, tonsil, throat, or external ear canal (1, 2). The pain is similar to that experienced with trigeminal neuralgia (TN) and can be triggered by eating, swallowing, and speaking. The pain of GPN can also be associated with hemodynamic instability and life-threatening syncopal episodes (3, 4). The median age at presentation is 50, and women are affected in about two thirds of cases (5). First-line treatment for GPN is usually medical therapy. Carbamazepine is frequently used, and if necessary additional agents such as gabapentin, phenytoin, and amitriptyline are added (6–8). When medical therapy no longer provides adequate relief or medications' side effects become intolerable, surgical intervention is considered (9, 10). Microvascular decompression for GPN is associated with high rates of pain relief (80%–90%) (9, 11, 12). However, surgical intervention carries a risk of permanent lower cranial nerve damage as high as 19% (13). We report a 99-year-old patient with GPN treated successfully with stereotactic radiosurgery.

CASE REPORT

A 99-year-old woman presented with an 18-month history of searing electric shock–like left facial, tongue, deep pharyngeal, and ear pain occurring at least 10 times a day and lasting 15 to 60 seconds per episode. The episodes of pain were triggered by talking, eating, drinking, and especially swallow-

ing and interfered with her quality of life, leading to a weight loss of 20 pounds over the 18 months prior to presentation. She was diagnosed with GPN and failed trials of gabapentin, pregabalin, carbamazepine, and oxcarbazepine due primarily to medication intolerance. She tolerated low doses of levetiracetam, but did not receive significant relief of her pain and experienced debilitating generalized weakness and syncopal episodes with dose escalation. She received two sphenopalatine blocks; the first provided pain relief for 6 weeks and the second for 4 days.

The patient was evaluated at Baylor University Medical Center at Dallas (BUMC) after she had been hospitalized for pain exacerbations and symptoms related to the dose escalation of levetiracetam. A detailed examination of her cranial nerves disclosed no abnormalities; magnetic resonance imaging (MRI) of the brain showed age-related ischemic white matter changes, but no evidence of extrinsic compression of the brainstem or cranial nerves. We recommended Gamma Knife radiosurgery for her GPN.

The treatment was performed on a Gamma Knife model 4C (Elekta Instruments) in the Baylor Radiosurgery Center at BUMC. The patient underwent stereotactic headframe placement under topical and injected local anesthetic. She underwent a T1 MRI with and without contrast with 1 mm slice thickness and zero interspace gap. A high-resolution computed tomography (CT) scan of the skull base was also obtained. The MRI and CT scan were imported into the treatment planning system (Leksell Gamma Plan, Elekta AB, Stockholm, Sweden) and fused. A three-dimensional stereotactic radiosurgery plan was created targeting the glossopharyngeal nerve at the glossopharyngeal meatus of the jugular foramen with a single shot with the 4 mm collimator (*Figure*). No plugging pattern was used. Targeting was confirmed on axial, sagittal, and coronal images. A dose of 40 Gy was given to the 50% isodose line, with a maximum dose of 80 Gy. The 50% isodose volume was 0.0895 cm³.

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Figure. Radiosurgical dose plan for the treatment of a patient with glossopharyngeal neuralgia. Axial CT images demonstrate a single 4-mm collimator isocenter in the glossopharyngeal meatus (*arrow*). The 50% isodose line, 40 Gy, is seen (*yellow circle*). Adjacent anatomy is seen including the jugular bulb (*asterisk*) and carotid canal (*arrowhead*).

The patient tolerated the treatment well, and there were no acute complications.

The patient experienced substantial pain relief 1 month following her Gamma Knife procedure. At 16 months posttreatment, she remained pain-free and off all medications for pain. She had no difficulty swallowing, speaking, eating, or drinking. Given her ability to eat without pain, she reported a marked

improvement in her quality of life. She experienced no acute or long-term adverse toxicity from Gamma Knife radiosurgery.

DISCUSSION

Compared with TN, GPN is a relatively uncommon craniofacial pain disorder. The incidence of TN is 28.9 cases per 100,000 person-years compared with only 0.4 cases per 100,000 person-years for GPN (14). While the characteristics of the pain are similar for both TN and GPN, with sudden severe stabbing pains usually lasting seconds to minutes with triggering events, the location is different. While TN affects the face in the V1, V2, and/or V3 distributions of the fifth cranial nerve, the pain from GPN is typically localized to the posterior tongue, throat/pharynx, and ear on the affected side. Additionally, while the diagnosis of both GPN and TN is clinical, GPN is more likely than TN to be associated with an underlying cause such as tumor or infection (15).

Destructive surgical interventions for GPN, including intracranial sectioning of the glossopharyngeal nerve, are associated with dysphasia. Microvascular decompression is a non-destructive surgical technique for GPN, with rates of complete pain relief in the range of 76% to 97% and a lower cranial nerve complication rate of 3% to 19% (5, 9, 11).

Stereotactic radiosurgery is a well-accepted treatment for patients with TN, with high rates of pain relief and low morbidity (16). Extrapolating from the favorable experience using radiosurgery for TN, a few centers have performed radiosurgery on patients with medically refractory GPN (*Table*). Worldwide, including the current study, only 15 patients have been reported

Table. Reported cases and outcome of patients with glossopharyngeal neuralgia treated with stereotactic radiosurgery

Authors, year	Age, gender	NVC	Target	Dose (Gy)	Outcome	Pain recurrence
Stieber et al, 2005	—, F	+	Cistern	80	Pain free, off medications	+ (FU 6 mos)
Lévêque et al, 2011						
Case 1	83, F	+	GPM	60	Pain free, off medication	+ (FU 7 mos)
Case 2	62, M	0	Cistern	70	Pain reduced 50%–90%	+ (FU 24 mos)
Case 3	66, M	+	Cistern	70	Pain reduced 50%–90%	+ (FU 24 mos)
Case 4	49, M	0	GPM	75	Pain free, off medication	0 (FU 32 mos)
Case 5	71, M	+	GPM	80	Pain free, off medication	Pain free, with meds (FU 13 mos)
Case 6	36, F	0	GPM	80	Pain free, off medication	0 (FU 10 mos)
Case 7	65, M	+	GPM	80	Pain free, off medication	Pain free, with meds (FU 8 mos)
Pollock & Boes, 2011						
Case 1		—	GPM	80	Pain free, off medications	0 (FU 19 mos)
Case 2		—	GPM	80	Pain free, off medications	0 (FU 16 mos)
Case 3	3M, 2F; Median age 61	—	GPM	80	Pain free, off medications	0 (FU 13 mos)
Case 4		—	GPM	80	Pain unchanged	—
Case 5		—	GPM	80	Pain unchanged	—
Williams et al, 2010	47, F	0	GPM	80	Pain free, off medications	0 (FU 11 mos)
Current report	99, F	0	GPM	80	Pain free, off medications	0 (FU 16 mos)

F indicates female; M, male; Cistern, cisternal segment of glossopharyngeal nerve; GPM, glossopharyngeal meatus; FU, follow up; NVC, neurovascular compression; mos, months; Gy, gray; —, no information available; +, yes; 0, no.

to receive radiosurgery for GPN. All patients were treated with the Gamma Knife.

The first report of GPN treated with radiosurgery was by Stieber et al for a patient with uncontrolled pain despite maximal medical management (17). The patient refused microvascular decompression and was offered Gamma Knife radiosurgery. The glossopharyngeal nerve root at its entry into the osseous canal of the jugular foramen was targeted. A maximum dose of 80 Gy was delivered with a single shot using the 4-mm collimator helmet. The patient had complete pain relief at 3 months without medication. However, at 6 months the pain recurred, less severe than before, and required no further intervention. The authors postulated that suboptimal coverage of the glossopharyngeal nerve at the entry into the jugular foramen may have contributed to pain recurrence.

A group from Marseilles reported seven patients with medically intractable GPN treated with radiosurgery (18, 19). Patients were treated with a range of doses (60, 70, 75, and 80 Gy). They observed a more durable response at radiosurgery doses ≥ 75 Gy and when targeting the glossopharyngeal meatus. The authors favored using the glossopharyngeal meatus as the target for GPN radiosurgery for three reasons: first, the opening of the jugular foramen is a good landmark well visualized on CT images; second, at this location the glossopharyngeal nerve is separated from the vagus and accessory nerves; and third, the distance from the brainstem allows higher radiosurgery doses (18). Pollock and Boes reported the results of five patients with medically resistant GPN who underwent Gamma Knife radiosurgery (13). Three patients were pain free and off medications at last follow up. Williams et al reported a case of a 47-year-old woman with medically refractory GPN who refused microvascular decompression and was successfully treated with Gamma Knife radiosurgery (20).

To date, 13 of 15 (87%) of reported patients treated with radiosurgery for GPN have achieved significant pain relief. Thus far, no adverse effects from stereotactic radiosurgery for GPN have been reported. The results tend to favor the glossopharyngeal meatus as the radiosurgery target for GPN. We chose the glossopharyngeal meatus as our target and found the CT useful for this purpose. As with any early and limited clinical experience, further study is warranted into areas of optimal radiosurgery targeting and dose for GPN. Similar dosing as that used for TN (~ 80 Gy) seems appropriate with a reasonable efficacy and side effect profile in reported cases (17, 18, 20).

Gamma Knife radiosurgery deserves particular consideration in the treatment of elderly patients with GPN. Our 99-year-old patient tried multiple medications and was hospitalized for life-threatening adverse effects linked to these medications. Sphenopalatine injections were only transiently effective, and she was deemed a poor candidate for surgery given her age.

Gamma Knife radiosurgery not only proved to be the only treatment option that she could tolerate, but also provided her with medication-free pain relief, which has continued for 16 months after treatment.

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