

Brief Communication

Repeat Trigeminal Nerve Radiosurgery for Refractory Cluster Headache Fails To Provide Long-Term Pain Relief

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Background.—Medically refractory cluster headache (MRCH) is a debilitating condition that has proven resistant to many modalities. Previous reports have indicated that radiosurgery for MRCH provides little long-term pain relief, with moderate/significant morbidity. However, there have been no reports of repeated radiosurgery in this patient population. We present our findings from the first reports of repeat radiosurgery for MRCH.

Methods.—Two patients with MRCH underwent repeat Gamma Knife radiosurgery at our institution. Each fulfilled clinical criteria for treatment, including complete resistance to pharmacotherapy, pain primarily localized to the ophthalmic division of the trigeminal nerve, and psychological stability. Both patients previously received Gamma Knife radiosurgery (75 Gy) for MRCH with no morbidity, but no long-term improvement of pain relief (Patient 1 = 5 months, Patient 2 = 10 months) after treatment. For repeat radiosurgery, each patient received 75 Gy to the 100% isodose line delivered to the root entry zone of the trigeminal nerve, and was evaluated post re-treatment. Pain relief was defined as: excellent (free of MRCH with minimal/no medications), good (50% reduction of MRCH severity/frequency with medications), fair (25% reduction), or poor (less than 25% reduction).

Results.—Following repeat radiosurgery, long-term pain relief was poor in both patients. Neither patient sustained any immediate morbidity following radiosurgery. Patient 2 experienced right facial numbness 4 months post re-treatment, while Patient 1 experienced no morbidity.

Conclusion.—Repeat radiosurgery of the trigeminal nerve fails to provide long-term pain relief for MRCH. Given the reported failures of initial and repeat radiosurgery for MRCH, trigeminal nerve radiosurgery should not be offered for MRCH.

Key words: refractory cluster headache, repeat gamma knife radiosurgery, trigeminal nerve, pain relief

(Headache **;***:**_**)

Medically refractory cluster headache (MRCH) is characterized by sudden onset of excruciating

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unilateral pain originating around the temple, eye, or cheek primarily along the ophthalmic division of the trigeminal nerve.⁷ Occurring in approximately 20% of cluster headache patients, MRCH poses significant challenges to patients and treating physicians alike.¹⁰ Multiple surgical modalities have been attempted, with the majority associated with significant morbidity and only modest clinical efficacy.^{3,5,12,13,15,21-24} Previous studies have investigated the role of radiosurgery to treat MRCH, yielding poor to moderate long-term efficacy and significant morbidity.^{1,2} However, there has been no report of repeat radiosurgery for MRCH. We report on 2 patients who previously underwent

radiosurgery for MRCH without efficacy who subsequently underwent repeat radiosurgery for MRCH.

CLINICAL MATERIALS AND METHODS

Patient Histories.—Patient 1 was a 41-year-old man with a 13-year medical history of right-sided MRCH for which he had taken verapamil, tegretol, neurontin, amitriptyline, lithium, valproic acid, and methadone unsuccessfully. His headaches were retroorbital in location, associated with tearing and redness of his right eye, and typically occurred 3 to 4 times per day, lasting 30 to 40 minutes in duration. Patient 2 was a 33-year-old man with a 30-month medical history of right-sided MRCH for which he had taken verapamil, desyrel, DHE-45, demerol, and capsaicin unsuccessfully. His headaches were frontotemporal and periorbital in location, typically occurring 15 to 20 times per month, each lasting 6 to 7 hours in duration, with a sufficient number of episodes lasting between 15 and 180 minutes to meet the International Classification of Headache Disorders criteria for chronic cluster headache.^{7,17}

Due to the intractability of their headaches despite prophylactic interventions, both patients chose to undergo Gamma Knife radiosurgery fully aware of the experimental nature of the procedure, as well as alternative treatments and side effects. Each patient's right trigeminal nerve was targeted with 75 Gy (collimator factor = 0.80, equivalent to 82 Gy with contemporary collimator factor of 0.87) to the 100% isodose line, using a model B gamma knife (Elekta AB, Stockholm, Sweden). Although there was no morbidity following treatment, neither patient experienced long-term pain relief. After a discussion of all alternative treatments, risk of failure and risk of side effects, each patient elected to undergo repeat radiosurgery of the trigeminal nerve.

Radiosurgical Re-treatment.—Both patients were admitted for outpatient radiosurgery to our gamma knife center. Each patient arrived on the morning of the procedure, and a stereotactic frame was applied under local anesthesia with intravenous sedation. The frame was oriented to make the base ring of the frame parallel to the trigeminal nerve axis.²⁰ Preoperative imaging systematically included magnetic resonance

(MR) and computed tomography (CT) scans. Axial MR sequences (Siemens 1.5 Tesla) included T2 high-resolution (0.5 mm) 3-dimensional acquisition and 3-dimensional T1 acquisition, as previously described.¹ CT bone window served to check and (when necessary) correct for potential MR distortion.² A single 4 mm collimator was used to target the cisternal segment of the nerve ipsilateral to symptom onset, defined as the portion between Meckel's cave and the pons. The anatomic target was the proximal trigeminal nerve, previously described as the radiosurgical target for essential trigeminal neuralgia and MRCH.^{1,2,9,19,20} Both patients received 75 Gy (collimator factor = 0.80) to the 100% isodose line, using a model B gamma knife (Elekta AB), as previously reported for trigeminal neuralgia.⁹

Post-Treatment Course.—Outcomes were divided into 4 pain relief categories, as previously described:^{1,2} excellent (free of MRCH with minimal/no medications), good (50% reduction of MRCH severity/frequency with medications), fair (25% reduction of MRCH), and poor (less than 25% reduction of MRCH). Although neither patient suffered any immediate morbidity, both patients experienced poor long-term pain relief outcomes. Patient 1 experienced no morbidity, but post re-treatment also had no pain relief. Thirteen days after repeat radiosurgery, Patient 2 was hospitalized 10 days for continuing MRCH. One month post re-treatment, he experienced good pain relief, which lasted 3 additional months until the headaches recurred, this time occurring 2–3 times per day, along with complaints of right facial numbness. Six months after re-treatment, he underwent a stereotactic right trigeminal glycerol neurolysis. Unfortunately, the patient continued to have no pain relief at 12 months after re-treatment. Neither patient experienced corneal reflex pathology, complete analgesia along the first division of the trigeminal nerve, or anesthesia dolorosa.

COMMENTS

The observation that invasive surgical approaches involving the trigeminal nerve provided moderate degrees of pain relief for MRCH patients^{5,8,12,13,24} led to the idea of using radiosurgery as a treatment

modality for this patient population, with the hope of avoiding the significant morbidity (corneal reflex damage, anesthesia dolorosa) directly proportional to the degree of pain relief reported with lesioning procedures such as percutaneous radiofrequency trigeminal rhizotomy (PRFR).^{13,16,21} Although an initial retrospective report indicated that trigeminal nerve radiosurgery could provide excellent pain relief for the majority of MRCH patients,² a subsequent prospective report involving more patients and a longer degree of follow-up concluded that the chances of long-term excellent pain relief following were minimal at best, and that the procedure carried a 50% risk of morbidity.¹ Due to these adverse findings, the latter study recommended that radiosurgery for MRCH may not be warranted.

The 2 patients in our report chose to undergo repeat radiosurgery during the 7-year span between the initial positive report and the subsequent negative findings regarding trigeminal nerve radiosurgery for MRCH. The findings of poor pain relief in both of our patients, combined with those of the aforementioned prospective study and our experience with long-term outcomes appear to emphatically indicate that radiosurgery of the trigeminal nerve is an inappropriate treatment option for MRCH, even when repeated more distally along the trigeminal nerve in the same patients.¹⁴ This finding is in stark contrast to the literature on repeat radiosurgery for trigeminal neuralgia, which has demonstrated a noticeable benefit for many patients who initially failed to experience pain relief following radiosurgery.^{6,18,25} Our findings, along with those from initial radiosurgery for MRCH with long-term follow-up and a study examining the long-term results of radiofrequency rhizotomy in the treatment of MRCH, lend support to the hypothesis that MRCH is central in origin, rather than peripheral.^{1,4,24} This reasoning has been supported by the recent success of deep brain stimulation (DBS) of the posterior hypothalamus for MRCH, which has provided comparable long-term pain relief with minimal morbidity compared with PRFR or alternative lesioning procedures.^{11,24} Given the low likelihood of the trigeminal nerve being involved in the origin of MRCH, the reasons for the failure of repeat trigeminal nerve radiosurgery for MRCH become evident.

CONCLUSION

In conclusion, our experience with the first 2 reported cases of repeat radiosurgery for medically refractory cluster headache revealed that repeat trigeminal nerve radiosurgery does not provide long-term pain relief for patients with poor pain relief following initial radiosurgery. Given the reported failures of initial and repeat radiosurgery for medically refractory cluster headache, trigeminal nerve radiosurgery should not be offered as a modality for this patient population.

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Conflict of Interest: None

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