NAGKC Project: Multi-Institutional Retrospective Analyses of Stereotactic Radiosurgery For Cavernous Sinus Cavernous Hemangiomas

PI and Co-PI of the Coordinate Institution (Taipei Veteran General Hospital, VGHTPE)

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Abstract
Cavernous sinus cavernous hemangioma (CSCH) is a kind of rare vascular tumor in cavernous sinus (CS). Direct microsurgical approach usually results in massive hemorrhage and incomplete tumor resection. Radiosurgery has emerged as a treatment alternative to microsurgery during the decades. Retrospective analyses of outcomes of radiosurgery for CSCH were published in limited and sparse series. The role of radiosurgery for the rare vascular tumors is still evolving. The study is aimed to elucidate the role of radiosurgery for CSCH by multi-institutional enrollment.

Keyword: cavernous sinus hemangioma, stereotactic radiosurgery, gamma knife radiosurgery, cavernous sinus

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Background

Cavernous sinus cavernous hemangioma (CSCH) is a kind of rare extra-axial vascular neoplasm that accounts for 2% to 3% of all cavernous sinus tumors. CSCH differs from the cavernous malformations in brain, namely that CSCH is a true vascular neoplasm and produces symptoms as a result of progressive tumor growth and mass effects. The optimal treatment strategy of CSCH is still controversial. Microsurgical approach may result in severe bleeding and even operative death, whereas total removal rate by surgical excision is only achieved in 30% to 44%. Difficulty in radical excision is mainly due to massive intra-operative hemorrhage or tumor adherence to the nearby neuromuscular structures. Postoperative cranial neuropathies, especially sixth cranial nerve injury, occur frequently because the nerve often lies within the tumor substance. If taking radiosurgery as the initial treatment, it can also help to reduce tumor size and vascularity to facilitate subsequent tumor removal by microsurgery. In 1999, Iwai et al reported the first CSCH case treated by Gamma Knife surgery (GKS). The tumor previously was partially removed by microsurgery, although severe intraoperative bleeding complicated the removal. Radiosurgery was performed as an adjuvant therapy for the patient, which resulted in dramatic tumor size decrease. Since then, 6 more reports have been published, all showing good response. In most reports, radiosurgery is used as adjuvant therapy after partial tumor removal. Radiosurgery has also been used as the primary treatment modality with good results in several patients. Moreover, from our previous data of GKS for various sellar and juxta sellar region tumors, it is found that the CSCH responded prompter with long-lasting tumor control compared with the others (Figures)

Specific aim

The purpose of this study is to clarify the efficacy and safety of GKS for CSCH. Imaging characters of CSCH on MRI, treatment parameters of GKS and the indications of treatment options (primary or adjuvant) and results are the factors for current analysis.

Importance

1. Define the efficacy of GKS for CSCH
2. Define the complications of GKS for CSCH
3. Analyze the prognostic factors of GKS for CSCH.
4. Establish the role of GKS for CSCH
5. Find out the image characteristics different between CSCH with other cavernous sinus tumors
Related publications

Since 1980, radiotherapy has been used as the adjuvant therapy in the subtotal removal of CSCH with effects. In 1999, Iwai et al reported the first CSCH treated with GKS. Since then, the treatment option has been propagated internationally. To date, 7 more reports related to GKS of CSCH have been published in the English literature, all of which show good response of CSCH to radiosurgery. In most reports, radiosurgery is used as adjuvant therapy for partially removed tumors, although it has been used as the primary treatment modality with good results in several patients. In 2000, Thompson et al reported a series of 4 CSCH patients treated with GKS. In the follow-up period of 6 months to 2 years, there was a mean 54% tumor reduction rate (range, 0%-86%). In 2001, Kida et al reported 3 CSCH treated by GKS with a mean follow-up time of 27 months. The mean tumor volume reduction was 57% (57%, 59%, and 54%, respectively). In 2008, Ivanov et al also reported 3 CSCH treated with GKS. Two of them underwent radiosurgery after partial resection of the tumors. In 2010, Chou et al reported a ever largest series of 7 CSCH treated with GKS and emphasized the possibility of the upfront GKS for CSCH by MRI diagnosis of CSCH. Two commentaries, Pollock and Regis, both agreed that the need for craniotomy and biopsy is generally not necessary for the majority of patients with a CSCH due to the distinctive imaging characteristics of CSCH. In order to further solidify the role of GKS for CSCH, we initiate the multi-institutional study.

Research Methods

Data Collection and Review:

1. Data Collection, in an anonymous manner, will include but not limited to the following: at initial. age, gender, clinical symptoms/signs, presenting neurological deficits, prior treatment for the lesions, prior hemorrhage, dose of radiation (Gy), dose planning, tumor location, number of months after radiosurgery, tumor size (cc), post intervention complications; Follow up: symptoms/signs, brain imaging, tumor size, brain edema, number of months until initial tumor progression, additional treatment (surgical resection, radiation, radiosurgery) if any, follow-up duration, and progression free survival etc.

2. An Excel spreadsheet file with all study parameters will be provided to each involved institution. Investigators in each involved institution are responsible for all diagnostic and therapeutic parameters that they provided. All filled spreadsheets will be centralized for analysis by the coordinate institution. The coordinate institution (VGHTPE) will review all data for completeness and prepare publication. The results of de-identified data will be shared with all involved institutions.

3. In order to ensure the homogeneity of imaging diagnosis for cases that GKS were used as an initial treatment and no pathological diagnosis is available throughout the study periods, the imaging core (formed by CCW, SCH, CJL,HMW,WYG) at VGHTPE are responsible for centralizing MR image reviewing. All involved institutions are responsible for providing diagnostic images for the reviewing.

Potential Institution to Involve:

1. University of Pittsburgh (Investigators: Dade Lunsford, M.D., Hideyuki Kano, M.D., Ph.D.)
2. University of Virginia (Investigator: Jason Sheehan, M.D., Ph.D.)
3. Washington Hospital, Fremont, CA (Investigator: David Larson, M.D., Ph.D.)
4. University of Sherbrooke (Investigator: David Mathieu, M.D.)
5. University of Winnipeg (Investigator: Anthony Kaufmann, M.D.)
6. Cleveland Clinic (Investigator: Gene Barnett, M.D.)
7. Hoag Memorial Hospital (Investigator: Christopher Duma, M.D.)
8. New York University Medical Center (Investigator: John Golfinos, M.D.)
9. University of Kentucky (Investigator: Byron Young, M.D.)
10. Mayo Clinic (Investigator: Bruce Pollock, M.D.)
11. NorthShore University Health System (Investigator: Gail Rosseau, M.D.)
12. University of California, San Francisco (Investigator: Mike McDermott, M.D.)
13. Yale University (Investigator: Veronica Chiang, M.D.)
15. Barrow Neurological Institute (Investigator: Heyoung McBride, M.D.)
16. Gamma Knife Center of Puerto Rico (Investigator: Carlos Carbini, MS)
17. Northwestern Memorial (Investigator: John Kalapurakal, M.D.)
18. Taipei Veteran General Hospital (Principle Investigator: Wen-Yuh Chung, M.D., Contact: Cheng-chia Lee, M.D.)

**Duration and time line:** Indefinite

**Statistical Analysis:**

1) Kaplan-Meier plots for progression-free survival; 2) univariate analysis on the Kaplan-Meier curves with log rank statistics; 3) multivariate analysis (Cox proportional hazards model or logistic proportional hazards model) for prognostic factors analysis. Standard statistical processing software (SPSS, version 15.0 and Prism, version 4.0) will be used.