Clinically Non-Functioning Pituitary Neuroendocrine Tumor radiosurgery

If surgical and/or medical therapy failed to control tumor growth, radiation therapy (RT) is currently the next treatment option. There are several RT options for patients with refractory PAs. Conventional external beam radiotherapy (EBRT) has been used to treat pituitary neuroendocrine tumors for several decades and has shown good clinical safety and efficacy. However, EBRT can result in significant complications, such as hypopituitarism, cognitive function deficiency and cerebrovascular disease (20). In recent years, EBRT has largely been replaced by stereotactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (FSRT). Stereotactic radiosurgery (SRS) is the delivery of a single high dose of radiation under conditions of accurate positioning. As new methods of radiation delivery, SRS and FSRT could minimize these complications. Recently, SRS has been gaining popularity because it minimizes the exposure of normal brain tissue to radiation. SRS has been preferred over EBRT because of the convenience of single-day therapy and the potential for a faster effect on the tumor [1)].

Case series

Zhang et al. retrospectively reviewed 45 elderly patients underwent GKRS as the initial treatment for NFPAs at our institution between December 2007 and December 2017. Patients' radiographic and clinical data were collected.

Results: The median age of patients at the time of GKRS was 71 years (range 65-82 years). The median tumor volume was 2.6 cm3 (range 0.3-21.8 cm3). The median marginal dose was 13 Gy (range 6-23 Gy). The median maximum dose to the optic apparatus was 6.5 Gy (range 2.3-10.3 Gy). Thirty-five patients (77.8%) achieved tumor regression, 6 patients (13.3%) had tumor stable and 4 patients (8.9%) occurred tumor progression during a median radiological follow-up time of 51.4 months (range 11.1-158.7 months). The crude tumor control rate was 91.1%. The actuarial tumor control rates were 100%, 95.0%, 87.6%, and 87.6%, at 1, 3, 5, and 10 years after initial GKRS, respectively. New-onset hypopituitarism occurred in 6 patients. Two patients with pre-GKRS visual dysfunction developed further deterioration of visual function. No other radiation-induced complications were noted.

Initial GKRS can provide a high tumor control rate as well as a low risk of postradiosurgical complications for elderly patients with NFPAs. Attention should be paid to avoid radiation-related adverse effects including hypopituitarism, optic neuropathy, and cranial neuropathy in elderly patients [2)].

Yamamoto et al. studied 27 patients (14 females, 13 males; mean age: 61 [range, 19-85] yr) who underwent SRS between 1998 and 2008 for NFPAs with such condition. The median tumor volume was 4.9 (range, 1.8-50.8) cc. To avoid excess irradiation to the OA, the lower part of the tumor was covered with a 50% or a 60% isodose gradient, ie 49% to 98% (mean, 84%; median, 88%) of the entire tumor received the selected doses. Median doses at the tumor periphery/OA were 7.6/11.0 (interquartile range [IQR], 5.8-9.1/10.1-11.8) Gy.

Seven patients (26%) were confirmed to be deceased due to unrelated diseases at a median post-SRS period of 149 (IQR, 83-158) mo. Follow-up magnetic resonance imaging (MRI) showed tumor growth in 2 patients (7%) at the 11th and 134th post-SRS months; the former underwent surgery and the other SRS. Excluding these 2 patients, the latest follow-up MRI examinations performed 13 to 238 (median: 168, IQR: 120-180) mo after SRS, showed no size changes in 5 (19%) and shrinkage in 20 (74%) patients. Cumulative incidences of tumor growth control were 96.3% and 91.8% at the 120th and 180th post-SRS months. None of our patients developed subjective symptoms suggesting SRS-induced optic neuropathy or endocrinological impairment.

In patients with NFPAs touching/compressing the OA, SRS achieves good long-term results [3].

Lee et al, evaluated the efficacy and safety of initial GKRS for NFAs.

An international group of three academic Gamma Knife centers retrospectively reviewed outcome data in 569 patients with NFAs.

Forty-one patients (7.2%) underwent GKRS as primary management for their NFAs because of an advanced age, multiple comorbidities, or patient preference. The median age at the time of radiosurgery was 69 years. Thirty-seven percent of the patients had hypopituitarism before GKRS. Patients received a median tumor margin dose of 12 Gy (range 6.2-25.0 Gy) at a median isodose of 50%. The overall tumor control rate was 92.7%, and the actuarial tumor control rate was 94% and 85% at 5 and 10 years postradiosurgery, respectively. Three patients with tumor growth or symptom progression underwent resection at 3, 3, and 96 months after GKRS, respectively. New or worsened hypopituitarism developed in 10 patients (24%) at a median interval of 37 months after GKRS. One patient suffered new-onset cranial nerve palsy. No other radiosurgical complications were noted. Delayed hypopituitarism was observed more often in patients who had received a tumor margin dose > 18 Gy ($p = 0.038$) and a maximum dose > 36 Gy ($p = 0.025$).

GKRS resulted in long-term control of NFAs in 85% of patients at 10 years. This experience suggests that GKRS provides long-term tumor control with an acceptable risk profile. This approach may be especially valuable in older patients, those with multiple comorbidities, and those who have endocrine-inactive tumors without visual compromise due to mass effect of the adenoma [4].

1)
Lee CC, Sheehan JP. Advances in Gamma Knife radiosurgery for pituitary tumors. Curr Opin Endocrinol Diabetes Obes. 2016 Aug;23(4):331-8. doi: 10.1097/MED.0000000000000269. Review. PubMed PMID: 27341278.
2)
Zhang L, Chen W, Ding C, Hu Y, Tian Y, Luo H, Chen J. Gamma Knife radiosurgery as the initial treatment for elderly patients with nonfunctioning pituitary neuroendocrine tumors. J Neurooncol. 2021 Feb 27. doi: 10.1007/s11060-021-03724-8. Epub ahead of print. PMID: 33638114.
3)
Yamamoto M, Aiyama H, Koiso T, Watanabe S, Kawabe T, Sato Y, Higuchi Y, Barfod BE, Kasuya H. Postsurgical Salvage Radiosurgery for Nonfunctioning Pituitary Adenomas Touching/Compressing the Optic Chiasm: Median 13-Year Postirradiation Imaging Follow-up Results. Neurosurgery. 2019 Oct 1;85(4):476-485. doi: 10.1093/neuros/nyy357. PubMed PMID: 30169702.
4)
Lee CC, Kano H, Yang HC, Xu Z, Yen CP, Chung WY, Pan DH, Lunsford LD, Sheehan JP. Initial Gamma Knife radiosurgery for nonfunctioning pituitary neuroendocrine tumors. J Neurosurg. 2014 Jan 3. [Epub

ahead of print] PubMed PMID: 24405068.