Gamma Knife radiosurgery for acromegaly

Numerous studies of radiosurgery for acromegaly have been carried out. These illustrate an overall remission rate of over 40%. Morbidity from radiosurgery is infrequent but can include cranial nerve palsies and hypopituitarism. Overall, stereotactic radiosurgery is a promising therapy for patients with acromegaly and deserves further study to refine its role in the treatment of affected patients [1)].

GKS is an effective adjuvant treatment option for remnant tumors inside the cavernous sinus (CS) after transsphenoidal surgery (TSS). Maximal surgical resection leaving a minimal volume of remnants only inside the CS allows the safe and sufficient delivery of a radiation dose to tumors, thereby increasing the possibility of remission. However, the risk of new hypopituitarism and radiation necrosis should be considered when tumors inside the CS are treated with GKS [2)].

Case series

Losa et al. performed a study to investigate, which would be the outcome of GKRS, independently on the response to somatostatin receptor ligand (SRL).

Design: Retrospective, observational study.

Patients: Ninety-six patients with active acromegaly were included.

Measurements: The cumulative probability of normalization of insulin-like growth factor 1 (IGF-1) levels after GKRS was assessed by the Kaplan-Meier method. The association of several clinical characteristics with GKRS outcomes was explored with the use of a Cox proportional-hazard model with the relative hazard ratio and 95% confidence interval (CI).

Results: Resistance to SRL occurred in 39 of the 96 patients (40.6%). After GKRS, patients resistant to SRL had a 5- and 10-year probability of remission of 40.7% (95% CI: 23.7%-57.7%) and 75.9% (95% CI: 57.9%-93.9%), respectively. Patients responding to SRL had a 5- and 10-year probability of remission of 46.8% (95% CI: 32.2%-61.4%) and 58.1% (95% CI: 41.5%-74.7%), respectively. The difference was not significant (p = .48 by the log-rank test). Multivariate Cox analysis confirmed that the only independent variables associated with GKRS outcome were basal growth hormone (GH; p = .001) and IGF-1 multiple of the upper limit of normal levels before GKRS (p = .013).

Conclusion: They demonstrate for the first time that the responsiveness to SRL has no effect on the probability to obtain remission of acromegaly after GKRS. The remission of disease occurred more frequently in patients who had lower GH and IGF-1 levels before GKRS [3)].

Forty-two patients (minimum 6 months follow-up) were included. The mean marginal dose was 27.7 (median 28, 20-35), and the mean BED received by the tumor was 193.1 Gy2.47 (median 199.7, 64.1-237.1). Based on the median values, we divided the patients into the high tumor BED group (H-BEDtm, 199.7-237.1 Gy2.47, n = 12) and low BED one (L- BEDtm, 64.1-199.7 Gy2.47 , n = 10). The two groups did not differ by pre-therapeutic IGF-1 levels (p = .1) or by the prescribed dose (p = .6).

Results: The mean follow-up period was 62.5 months (median 60.5, 9-127). The probability of IGF-1

normalization was 65% at 3 years and 72.4% at 4 years, remaining stable until last follow-up. Twenty-two (52.4%) patients had complete endocrine remission in absence of any Somatostatin analogs. Actuarial rates were 33% at 3 years and 57.4% at 7 years, further remaining stable during the follow-up course. In univariate analysis, the only statistically significant parameter was pre-therapeutic serum IGF-1 and IGF-1 index (p = .01). Five patients (5/26, 19.3%) without previous hypopituitarism developed new pituitary insufficiency. H-BEDtm was associated with higher rates of endocrine remission compared with L-BEDtm, with an actuarial probability of 70.2% versus 48.2% at 9 years, although this did not reach statistical significance (p > .05).

The study confirms that SRS by Gamma Knife is safe and effective for GH-secreting PA. Pre therapeutic serum levels of IGF-1 were the only statistically significant parameters for endocrine remission [4].

A retrospective analysis of hormonal, radiological, and ophthalmologic data collected in a predefined protocol from 1994 to 2009. The mean age at treatment was 42.3 years (range 22-67 yy). 103 acromegalic patients participated in the study. The median follow-up was 71 months (IQ range 43-107). All patients were treated with GK for residual or recurrent GH-secreting adenoma. Results. Sixty-three patients (61.2%) reached the main outcome of the study. The rate of remission was 58.3% at 5 years (95% CI 47.6-69.0%). Other 15 patients (14.6%) were in remission after GK while on treatment with somatostatin analogs. No serious side effects occurred after GK. Eight patients (7.8%) experienced a new deficit of pituitary function. New cases of hypogonadism, hypothyroidism and hypoadrenalism occurred in 4 of 77 patients (5.2%), 3 of 95 patients (3.2%), and 6 of 100 patients at risk (6.0%), respectively. Conclusion. In a highly selected group of acromegalic patients, GK treatment had good efficacy and safety [5].

Thirty acromegalic patients (14 women and 16 men) entered a prospective study of GK treatment. Most were surgical failures, whereas in 3 GK was the primary treatment. Imaging of the adenoma and target coordinates identification were obtained by high-resolution magnetic resonance imaging. All patients were treated with multiple isocenters (mean, 8; range, 3-11). The 50% isodose was used in 27 patients (90%). The mean margin dose was 20 Gy (range, 15-35), and the dose to the visual pathways was always less than 8 Gy. After a median follow-up of 46 months (range, 9-96), IGF-I fell from 805 micro g/liter (median; interquartile range, 640-994) to 460 micro g/liter (interquartile range, 217-654; P = 0.0002), and normal age-matched IGF-I levels were reached in 7 patients (23%). Mean GH levels decreased from 10 micro g/liter (interquartile range, 6.4-15) to 2.9 micro g/liter (interquartile range, 2-5.3; P < 0.0001), reaching levels below 2.5 micro g/liter in 11 (37%). The rate of persistently pathological hormonal levels was still 70% at 5 yr by Kaplan-Meier analysis. The median volume was 1.43 ml (range, 0.20-3.7). Tumor shrinkage (at least 25% of basal volume) occurred after 24 months (range, 12-36) in 11 of 19 patients (58% of assessable patients). The rate of shrinkage was 79% at 4 yr. In no case was further growth observed. Only 1 patient complained of side effects (severe headache and nausea immediately after the procedure, with full recovery in a few days with steroid therapy). Anterior pituitary failures were observed in 2 patients, who already had partial hypopituitarism, after 2 and 6 yr, respectively. No patient developed visual deficits. GK is a valid adjunctive tool in the management of acromegaly that controls GH/IGF-I hypersecretion and tumor growth, with shrinkage of adenoma and no recurrence of the disease in the considered observation period and with low acute and chronic toxicity [6].

149 patients with GH-secreting pituitary neuroendocrine tumor, 97 males and 52 females, aged 42.8 (12-72 years), with a course of 6-240 months (72.5 months) and with the mean volume of tumor of 2.36 cm(3) (0.11-12.7 cm(3)) were treated by GKS. The mean dose to tumor margin was 20.87 Gy (10-30 Gy). 124 of them were followed up for 30 months (6-72 months).

The serum GH returned normal in 74 patients (64.9%) and declined in comparison with the level before radiosurgery in 23 patients (18.5%). The tumor volume was reduced in 84 patients (67.7%) and remained unchanged in 124 patients (32.4%). Ambiopia appeared in one patient. No other complication was found during the follow-up.

GKS is safe and effective on the treatment of GH-secreting pituitary neuroendocrine tumor [7].

1)
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