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Diplopia outcomes following stereotactic radiosurgery for petroclival or cavernous sinus meningiomas: patient series

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BACKGROUND Skull base meningiomas (SBM) often present with diplopia due to compression of the abducens cranial nerve (CN VI). The authors evaluated outcomes in 13 patients diagnosed with SBMs who were experiencing diplopia to determine if Gamma Knife surgery (GKS) resulted in resolution of their symptoms.

OBSERVATIONS Fourteen patients who were diagnosed with SBMs located in the cavernous sinus, clivus, or petroclival regions and presented with diplopia were treated by GKS. Demographic and clinical data as well as the duration of diplopia prior to GKS were documented. Of the 13 patients included in the study, 1 was excluded because he was lost to follow-up. For the remaining 12, diplopia was resolved in 10 (83%) and no change was noted in 2 (17%). Time to resolution was measured in months, varying from 1 to 30 months, with a median resolution time of 4.5 ± 9.7 months. Of the patients with documented postradiosurgical resolution (n = 10), the median amount of time with diplopia prior to GKS was 1.5 months (range, 1 to 20).

LESSONS This study showed that diplopia, related to a basal meningioma, may improve following GKS. An earlier time course to radiosurgery after diplopia onset was associated with better outcomes.

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KEYWORDS skull base meningioma; radiosurgery; abducens nerve palsy; diplopia

Skull base meningiomas (SBMs), including petroclival and cavernous sinus meningiomas, comprise 35%–50% of all intracranial meningiomas seen clinically. Upon expansion, they can apply pressure onto cranial nerves (CNs), causing symptoms that vary among facial numbness, pain, muscle weakness, and diplopia.[1] This study focused primarily on meningioma-related diplopia and its resolution following GKS on the offending lesion. These tumors, located in the cavernous sinus, clivus, or petroclival regions, pose a difficult challenge for maximal resection because of their proximity to vital neurovascular areas.[2] Although strides have been made in improving outcomes, this former approach often yielded a low resection rate and high recurrence rate.[3] Stereotactic radiosurgery (SRS), on the other hand, is a widely accepted approach for small SBMs because of reported outcomes rates.

The intention of this study was to analyze the evolution of SBM-induced diplopia following GKS. The study was designed as a retrospective case-control study.

Study Description

This study was carried out under the approval of the New York University Institutional Review Board. The patient records were prospectively documented and retrospectively examined and reviewed. Physical examinations were performed on the patients prior to diagnosis to confirm the presence of diplopia and at follow-up after single-session GKS to confirm the resolution of diplopia. Self-reporting to the physician's office about diplopia resolution was also considered in this study. All but 2 patients completed each examination or self-reported their condition improvement. Mean, median, and standard deviation calculations were used to analyze the data concerning duration of diplopia prior to GKS, time to resolution, and age at the time of surgery.

Observations

Our study population included 13 patients with a mean age of 54 ± 9 years; of these patients, 10 (77%) were female (Table 1).

ABBREVIATIONS CN = cranial nerve; GKS = Gamma Knife surgery; SBM = skull base meningioma; SRS = stereotactic radiosurgery.

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TABLE 1. Demographic and clinical parameters of the study population (n = 13)

Case No.	Age (yrs)	Sex	Tumor Location	Mos of Diplopia Prior to GKS	Tumor Vol, cc	Margin Dose, Gy	Mos to Diplopia Resolution	Adjuvant Steroids
1	63	M	Cavernous sinus	NA	6.4	13	Lost to FU	Yes
2	36	F	Cavernous sinus	13	13.9	20/5 fractions	7	No
3	66	M	Cavernous sinus	1	3.3	13	1	No
4	47	F	Petroclival	2	7.2	13	6	No
5	54	F	Cavernous sinus	1	18.2	11	20	No
6	59	F	Cavernous sinus	1	2.8	13	NR	No
7	55	F	Cavernous sinus	4	5.5	12.5	3	No
8	41	M	Petroclival	1	0.9	12.5	1	Yes
9	61	F	Petroclival	1	1.2	12.5	1	Yes
10	65	F	Cavernous sinus	9	3.5	12	NR	No
11	51	F	Cavernous sinus	1	5.2	12.5	1	Yes
12	51	F	Cavernous sinus	2	5.6	12.5	30	No
13	49	F	Petroclival	20	3.2	12	7	Yes

FU = follow-up; NA = not applicable; NR = no resolution.

Prior to surgery, 4 patients presented with a meningioma in the petroclival region (29%) and 9 were found to have a meningioma in the cavernous sinus (69%), of whom 1 was lost to follow-up. Twelve patients were treated by single-session SRS with a median prescription dose of 12.5 Gy (range, 11–13), while 1 patient received fractionated therapy to preserve optic functions. Of the 12 patients being followed, diplopia was resolved in 10 (83%) and no change was noted in 2 (17%). Resolution time was versatile, with a median resolution time of 4.5 months (range, 1–30 months). The average period of having diplopia prior to GKS was 4.7 months (± 6.2). Figure 1 shows a case of a 61-year-old woman with petroclival meningioma who experienced resolution of her diplopia within 1 month after GKS as well as tumor reduction over a follow-up period of 22 months. Two patients experienced diplopia for longer than 10 months and still achieved diplopia improvement. Of the 12 patients being followed, 4 (33.33%) were given adjuvant steroid treatment, which was tapered down over several weeks. All 4 patients showed resolution of their diplopia, in comparison to 6/8 (75%) who did not receive adjuvant steroids ($p = 0.273$; chi-square). Average resolution time among the steroid-treated group was 2.5 months (± 3) in comparison to 11 months (± 11) in the nonsteroid group ($p = 0.122$; Mann-Whitney nonparametric test). Two patients did not experience resolution of their diplopia, which lasted 1 months in one case and 9 months in the other, prior to treatment. Both patients had cavernous sinus tumors.

Discussion

The results of this study indicate that GKS treatment for associated meningiomas compressing CN VI in the cavernous sinus, clivus, or petroclival regions can resolve or significantly improve diplopia in most patients (83%). The lateral rectus muscle is innervated by the abducens nerve (CN VI), and palsy of this nerve causes horizontal diplopia, which is typically more affected on the side on which the tumor resides.[4]

Observations

Our results demonstrate higher rates of improvement in abducens nerve palsies in comparison to previous studies that showed variable rates of improvement, depending on tumor type, location, and dose. Roche et al. reported a 60% improvement rate among 10 patients who were treated by 13 Gy (range, 10–15) GKS for petroclival meningiomas and suffered from preradiosurgical 6th nerve deficits (2 improved and 4 recovered).[5] The same group also reported of a 42% improvement rate in 6th nerve palsy among 33 patients who received GKS for cavernous sinus meningiomas.[6]

In a study completed by Faramand et al., tumor control was evaluated after SRS in 104 patients for both residual and recurrent tumors. At median follow-up time of 75 months, tumor control was achieved in 90% of patients, but only 19% reported a CN function improvement, and 10% even reported a deterioration in CN function.[7] This finding demonstrates that although tumor control is high in SRS, diplopia recovery may not always be related to tumor reduction.

The locations of these meningiomas pose risks for resection by traditional microsurgical techniques and, due to a superior safety profile, GKS is considered the gold standard for treatment.[8] Open microsurgical resection of meningiomas can potentially cause complications such as motor, visual, language, and cognitive deficits as well as seizures and CN deficits.[9] Gozal et al. found that in a study of 50 patients, microsurgery showed no improvement in 46% of cases and actually worsened symptoms such as visual deficits, headaches, and proptosis in 2% of cases. In the same study, it was reported that 12 new CN deficits emerged in 10 patients (20%) who underwent microsurgical decompression.[10]

In comparison, new post-GKS neuropathies are uncommon, and the occurrence of a new deficit depends on the dose delivered to the specific nerve tissue and the exposed segment's length.

Morita et al. followed 88 patients who received GKS for SBM and reported only one case of new abducent neuropathy that developed 7 months after administering a dose of 22 Gy for a cavernous meningioma.[11]

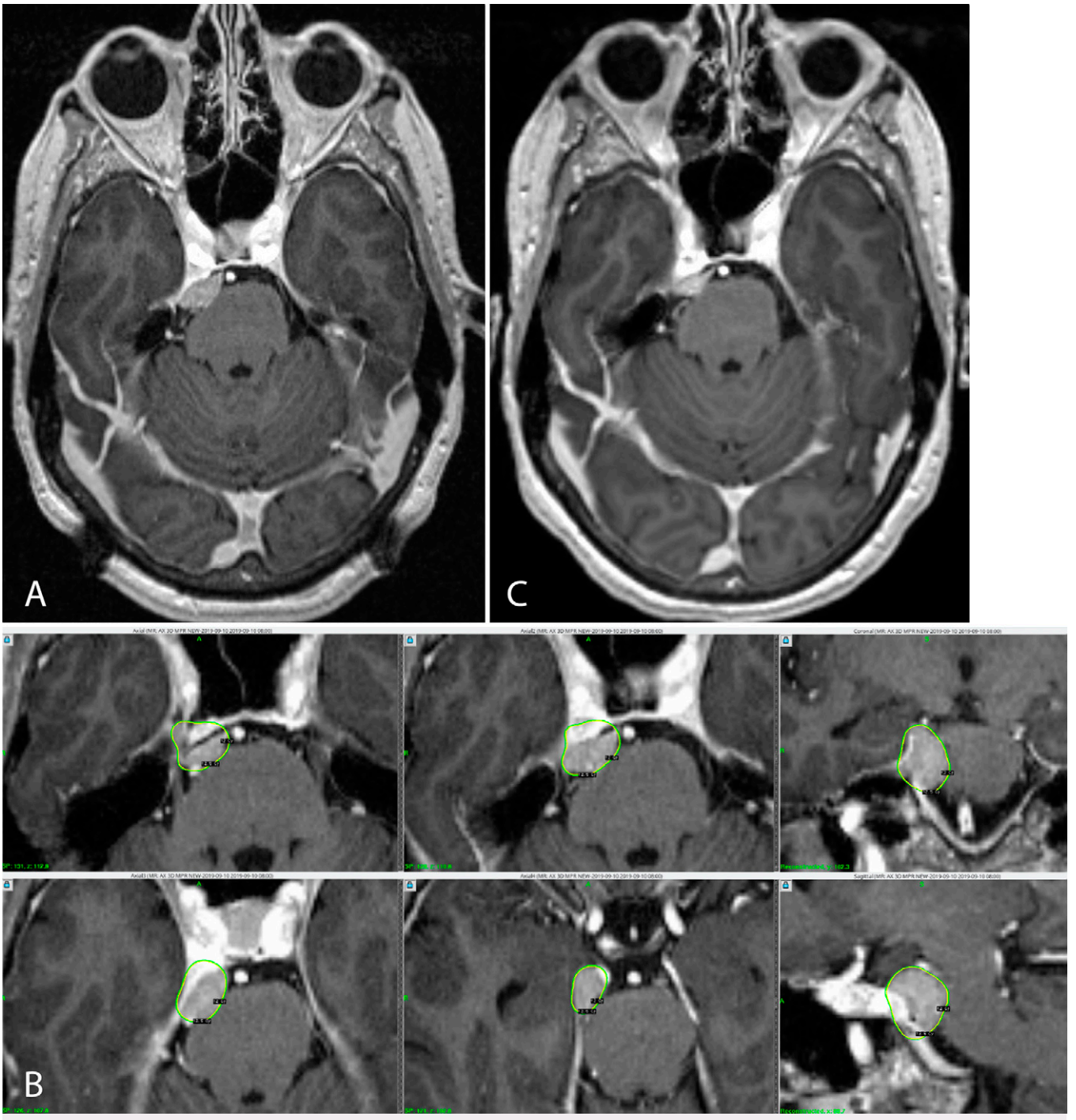

FIG. 1. Case 10. Axial T1-weighted magnetic resonance imaging for GKS in a 61-year-old woman with a petroclival meningioma. Diplopia resolved within 1 month after surgery. Images with contrast before (**A**) and during radiosurgery using 12.5 Gy to the 50% isodose line (**B**). 20 months later, the tumor had regressed (**C**).

Furthermore, in a study conducted by Cifarelli et al. comprising 217 patients, only 9 (4%) in the sample were found to have any new CN dysfunctions, and 66% of those afflicted reported eventual resolution of symptoms. Three patients (1.4%) sustained new or worsening postradiosurgical abducent neuropathy. In addition, patients with a history of prior GKS were noted to be at higher risk for developing CN dysfunction.[12]

In our study, the alleviation of diplopia was shown to occur in a timely manner of median 4.5 months for those who showed improvement. Many patients underwent GKS in 4 months or less after diagnosis of diplopia; however, 2 patients suffered from diplopia for longer than 10 months and GKS still resulted in a return of their normal vision. It is possible that microscopic changes, such as

restoration of axoplasmic flow following GKS, are responsible for the early resolution of cranial neuropathies, yet it should be noted that spontaneous resolution of 6th nerve palsy in skull base tumors had been described.[13]

Four of the 12 treated patients were given adjuvant steroid treatment that was tapered down over several weeks, and all experienced a resolution in their diplopia. We also noticed a statistically nonsignificant trend toward faster resolution of symptoms among patients who were treated with steroids ($p = 0.122$). Jessurun et al. demonstrated in a systematic review that administration of dexamethasone, in particular, may lead to a decrease in intracranial pressure as well as edema volume decrease.[14] Steroid treatment may be a confounding variable resulting in improvement of diplopia due to a reduction of pressure on CN VI. In a study of 15 highly selected patients experiencing idiopathic 3rd and 6th CN palsy, 9 received steroid treatment. Those who received steroid treatment responded well and were deemed to have the best prognosis of those in the sample, leading authors to believe that steroid treatment is an effective therapy, at least temporarily, for idiopathic CN VI dysfunction.[15]

Limitations

The main limitation of this study is its small size, which made it difficult to perform subgroup analysis and statistical comparisons. For instance, we believe that a larger study may have revealed a statistically significant effect of steroids on the rate of diplopia resolution. Furthermore, the study's retrospective nature may have resulted in a recall bias regarding dates of symptoms onset and resolution.

Lessons

We believe that the benefits of GKS are not just in stopping tumor growth but in alleviating diplopia related to the tumor. This information should be discussed with patients while weighing therapeutic options, such as microsurgical resection or clinical follow-up. Further larger and prospective studies are imperative to validate our findings.

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Author Contributions

Conception and design: all authors. Acquisition of data: all authors. Analysis and interpretation of data: Berger, Kondziolka. Drafting the article: Berger, Kondziolka. Critically revising the article: Kondziolka. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Berger. Statistical analysis: Berger, Levy. Study supervision: Levy, Kondziolka.

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