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Case Report

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# Efficacy of Gamma Knife Radiosurgery In The Treatment of Metastatic Parapharyngeal Acinic Cell Adenocarcinoma In The Cavernous Sinus: A Case Report

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## Abstract

Metastatic acinar cell adenocarcinoma (ACA) of the salivary gland involving the cavernous sinus is rare. We report a case highlighting the efficacy of gamma knife radiosurgery for treating metastatic lesions in the right cavernous sinus from a primary correct para pharyngeal acinic cell adenocarcinoma. This is the first reported case of treatment of such a tumor with gamma knife radiosurgery, in which tumor control was achieved.

## Introduction

Acinic cell adenocarcinoma arising in the salivary glands is an uncommon tumor, accounting for 2 % to 5 % of primary parotid gland neoplasms1. They are considered low-grade malignant tumors, most commonly occurring during the fifth and sixth decades of life, with a gender predilection of women more than men **[1]**. Treatment typically consists of surgery and adjuvant radiotherapy. Although the metastatic tendency of such a tumor to distant sites such as lungs, bones, orbit, and liver has been well documented in the literature, metastatic disease to the cavernous sinus without direct intracranial extension is rare. Douglas JG et al. **[2]** demonstrated that treating primary salivary gland neoplasms involving the base of the skull with gamma knife surgery following neutron radiotherapy improves local control and adds little additional toxicity. However, to our knowledge, the treatment of metastatic ACA to the cavernous sinus with gamma knife radiosurgery alone remains unreported in international literature.

## Case Report

A 39-year-old female patient was diagnosed with a right para pharyngeal Acinic Cell Adenocarcinoma in 2012 and had undergone a right parotidectomy and resection of the lesion via both a trans parotid and transcervical approaches by the Ear, Nose, and Throat (ENT) specialist. 9 months after the initial surgery, the routine surveillance Magnetic Resonance Imaging (MRI) of the nasopharynx and neck demonstrated a local recurrence, for which a repeat resection was performed. This was followed by adjuvant radiotherapy of 69.96 Gray (Gy) over 33 fractions to the remnant tumor.

There was no evidence of tumor recurrence on the follow-up MRIs in the following years. However, the MRI 5 years after the initial diagnosis revealed a new lesion in the left inferior alveolar canal measuring 0.5 x 1.0 cm, which further progressed to a size of 0.6 x1.4cm 6 months later. The enlarged lesion appeared well-defined with smooth scalloped margins and did not exhibit cortical disruption or infiltration of the marrow spaces or the adjacent extra-osseous soft tissue component. These features were indicative of a non-aggressive lesion.

She initially declined the biopsy but subsequently developed pain over the left mandibular nerve dermatome distribution, dizziness, nausea, and photophobia. However, there was no clinical evidence of ophthalmoplegia.

A repeat MRI in March 2018 revealed a 1.0 x 0.9 cm lesion within the posterior aspect of the right cavernous sinus seen on the T1 weighted with contrast sequence **(Figure 1)**. The lesion in the left mandible had also progressed in size. A retrospective review of the MRI performed 6 months earlier suggested that the lesion in the cavernous sinus was already present then and measured 0.5 x 0.5 cm. The patient was therefore referred to the neurosurgery clinic for management of metastatic acinic cell adenocarcinoma to the right cavernous sinus.

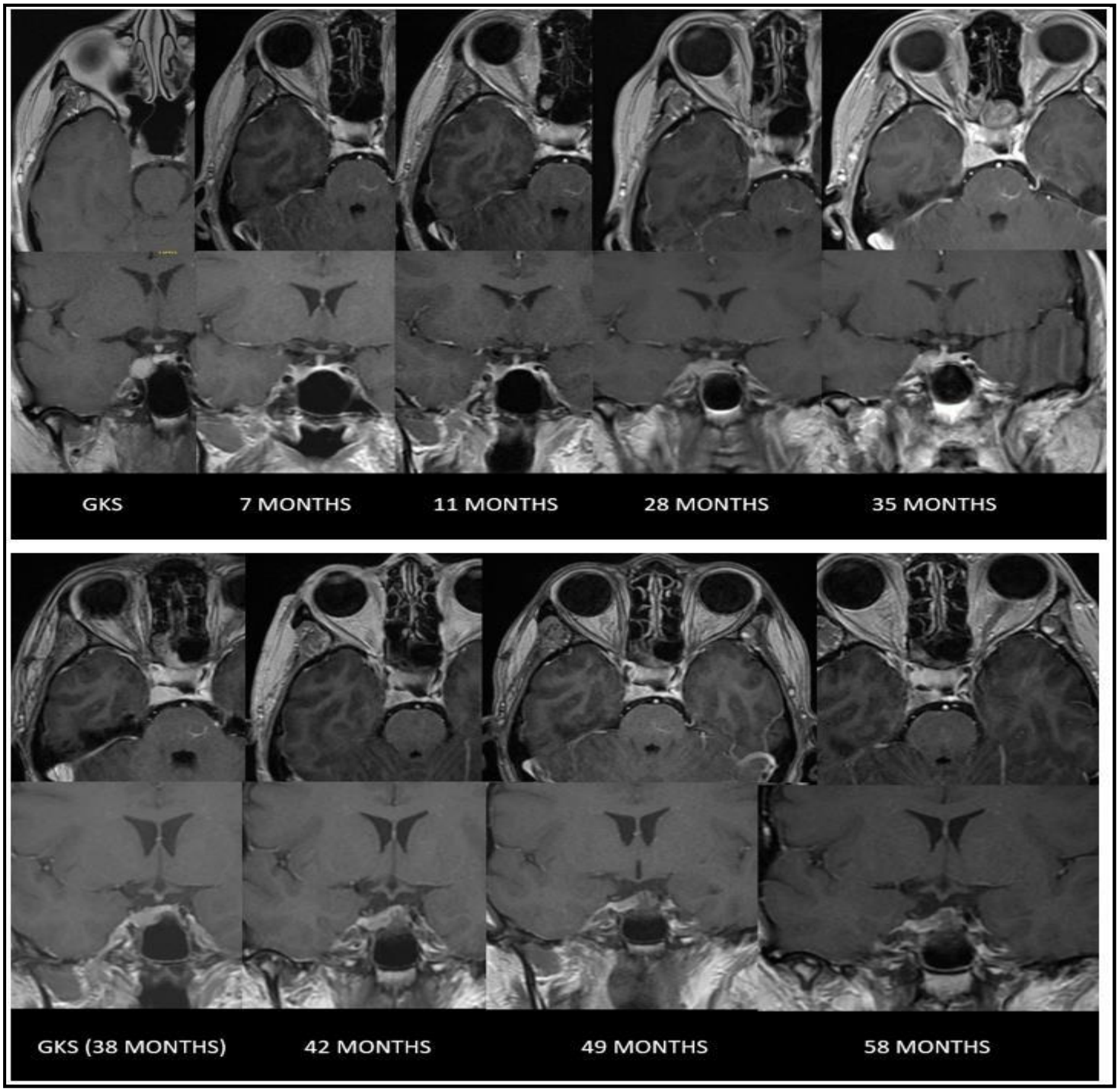


**Figure 1:** MRI Brain (T1 weighted with contrast) images showing the sizes of the right cavernous sinus lesion on follow-up serial imaging.

As a result of worsening pain, she had agreed to undergo an incisional biopsy of the left mandibular lesion in April 2018 by the oral maxillofacial surgery team. The histology demonstrated an ACA with identical features to that seen in the specimen from the first surgery and confirmed that there were no high-grade features or features of dedifferentiation.

Positron emission tomography–computed tomography (PET-CT) showed fluorodeoxyglucose (FDG) avidity in the left mandibular ramus but demonstrated no evidence of local recurrence over the right parapharyngeal surgical site, nor was there cervical node involvement.

The definitive histological diagnosis of the cavernous sinus lesion was not obtained as the patient had refused biopsy. As discussed in the neuro-oncology multidisciplinary team meeting, the presumptive diagnosis was a metastatic lesion within the cavernous sinus, likely originating from the primary para pharyngeal ACA. This was based on her history of recurrent ipsilateral parapharyngeal ACA, the progression of the large sinus lesion evident on serial MRI scans, and its temporal association with a biopsy-proven metastatic ACA of the contralateral mandible. The patient, however, remained asymptomatic from the cavernous sinus lesion.

The patient decided to undergo stereotactic radiosurgery using Gamma Knife Radiosurgery (GKRS, Leksell Gamma Knife® Perfexion) to the cavernous sinus lesion in May 2018 **(Figure 2)**. The volume of the tumor was 1.1cc at the time of GKRS planning and the prescription radiation dose was 18 Gy to 96 % tumor coverage. The optic apparatus received a radiation dose of less than 3 Gy, while the amount to the pituitary was between 3 to less than 18 Gy. She was discharged stable and well on the same day.

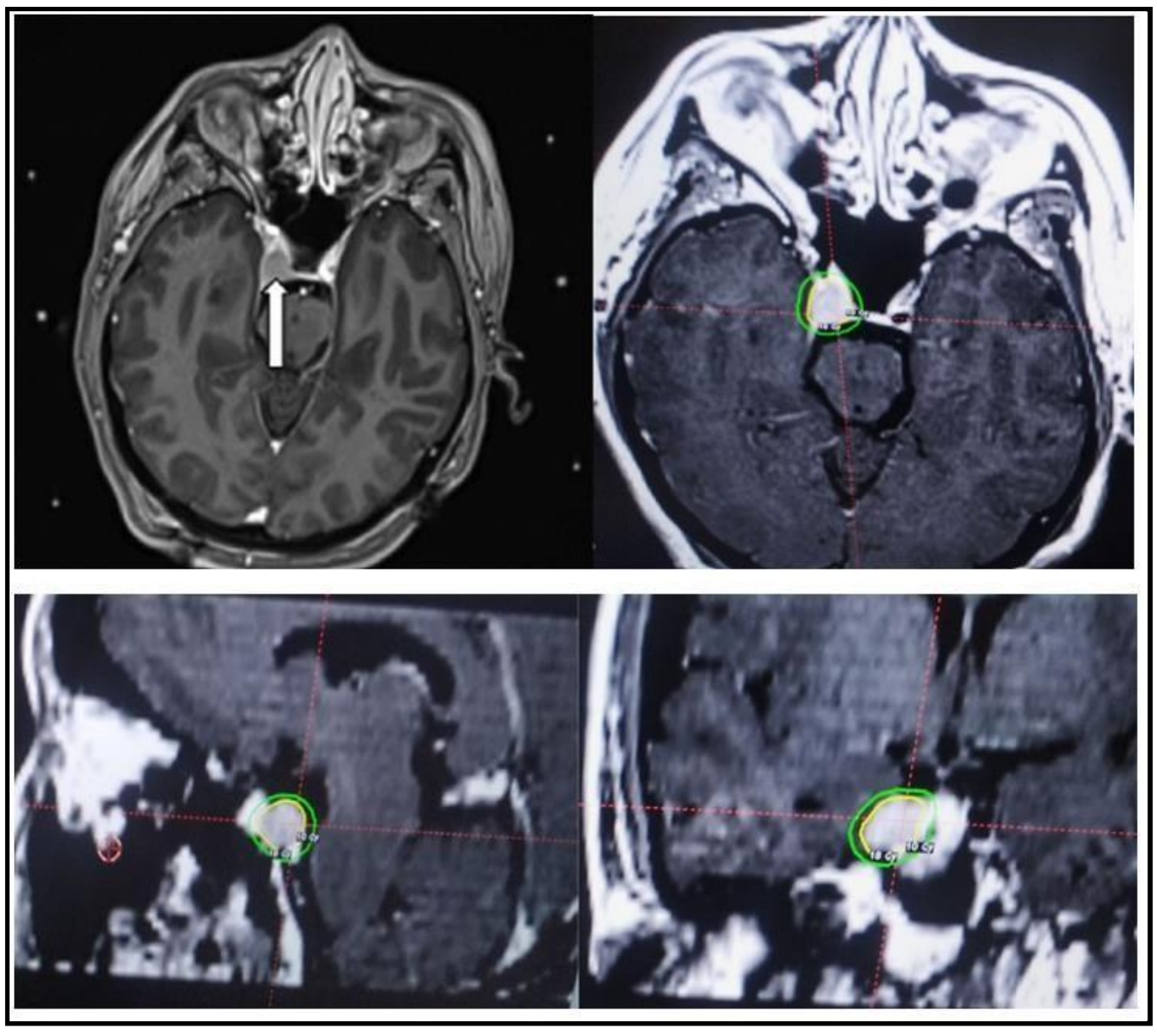

**Figure 2:** MRI performed for Gamma knife radiosurgery planning in May 2018.

She then underwent a left mandibulectomy and fibula-free flap reconstruction of the mandible a month after the frame-based radiosurgery, and this was again followed by adjuvant radiotherapy of 60 Gy over 30 fractions to the remnant mandibular tumor. In the months following GKRS, the patient did not experience any complications related to gamma knife radiosurgery, specifically ophthalmoplegia, given the proximity of the lesion to the optic apparatus. The lesion within the cavernous sinus had responded well to gamma knife radiosurgery, as evidenced by a decrease in tumor volume of 0.85cc based on surveillance MRI performed 5 months after GKRS, and further decreased to a book of 0.1cc nearly 1 year after initial radiation.

Serial imaging 28 months after radiosurgery demonstrated that the lesion had unfortunately increased to a volume of 0.83cc. The lesion progressed to 0.99cc in the book, and the patient underwent another session of GKRS 38 months after the initial radiosurgery. Similarly, an 18Gy to 96 % tumor coverage was the prescribed dose, and the maximum radiation dose to any part of the optic apparatus was less than 6 Gy, while the amount to the pituitary again varied between 3 to less than 18 Gy.

A follow-up MRI Brain with contrast done 3 months after the second session of GKS showed that the right cavernous sinus lesion had halved in size to a volume of 0.48cc compared to the previous MRI scan done during the GKRS planning. A pituitary hormonal profile done in October 2021 as part of the follow-up had also returned to normal. The latest MRI Brain with contrast performed 58 months after the first radiosurgery session demonstrated a tumor volume of 0.1cc, significantly smaller than the volume at the initial diagnosis. **Figure 3** illustrates the change in tumor volume over time in years. 63 months since the initial session of gamma knife radiosurgery, and the patient remains well and has not experienced any side effects or complications related to Gamma Knife Radiosurgery.

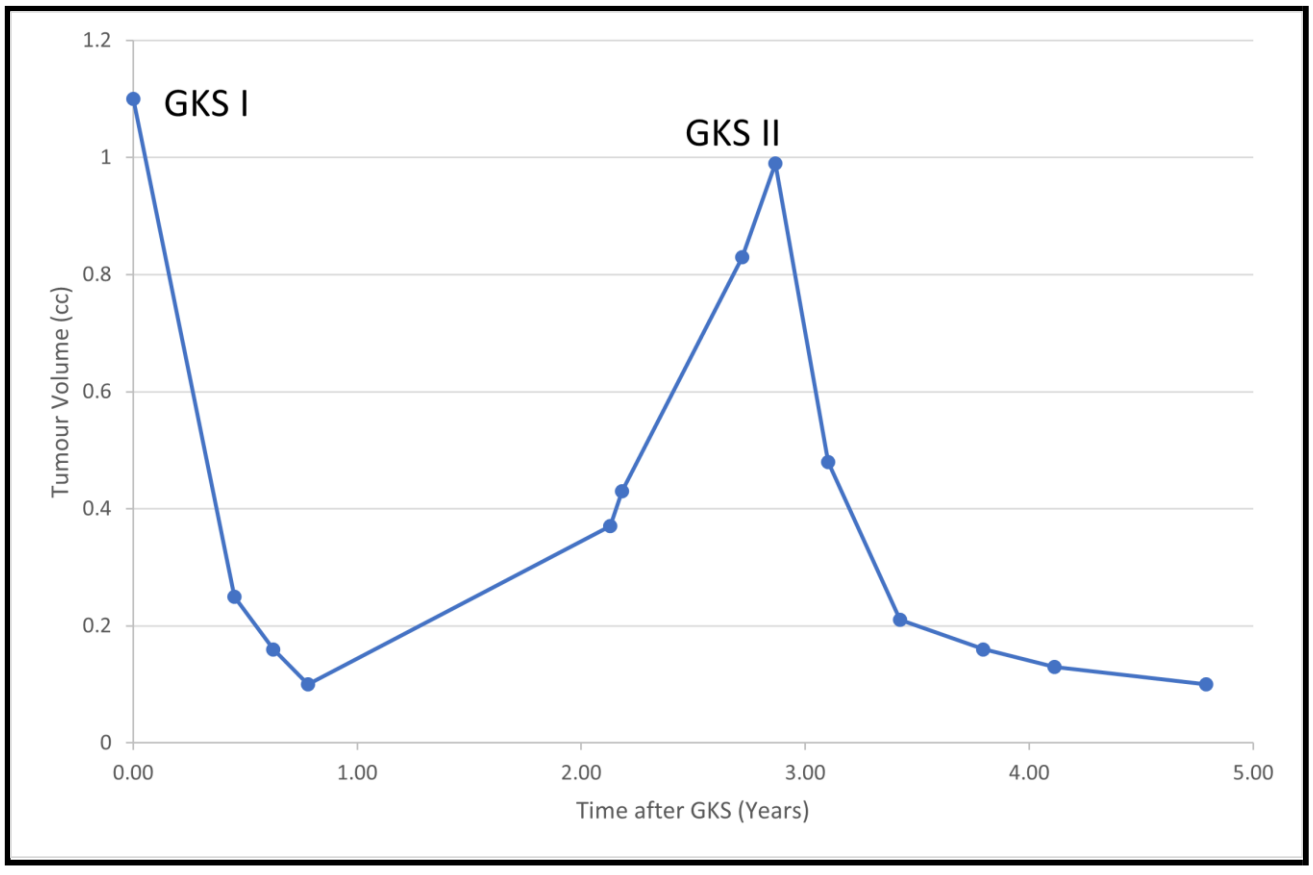


**Figure 3:** Graph demonstrating the change in tumour volume over time in years.

## Treatment data:

Prescription dose GKS I: 18 Gy to 96 % tumour coverage= 19 Gy to 90 % tumour coverage.

Prescription dose GKS II: 18 Gy to 96 % tumour coverage= 19 Gy to 90 % tumour coverage.

| | | Tumour volume (cc) | | Time after GKS |
|---|---|---|---|---|
| 2018-05-04 | 2018-05-04 | 1.1 | 0 | 0.00 |
| 2018-05-04 | 2018-10-16 | 0.25 | 165 | 0.45 |
| 2018-05-04 | 2018-12-18 | 0.16 | 228 | 0.62 |
| 2018-05-04 | 2019-02-13 | 0.1 | 285 | 0.78 |
| 2018-05-04 | 2020-06-19 | 0.37 | 777 | 2.13 |
| 2018-05-04 | 2020-07-08 | 0.43 | 796 | 2.18 |
| 2018-05-04 | 2021-01-20 | 0.83 | 992 | 2.72 |
| 2018-05-04 | 2021-03-15 | 0.99 | 1046 | 2.87 |
| 2018-05-04 | 2021-06-09 | 0.48 | 1132 | 3.10 |
| 2018-05-04 | 2021-10-04 | 0.21 | 1249 | 3.42 |
| 2018-05-04 | 2022-02-17 | 0.16 | 1385 | 3.79 |
| 2018-05-04 | 2022-06-13 | 0.13 | 1501 | 4.11 |
| 2018-05-04 | 2023-02-15 | 0.1 | 1748 | 4.79 |

## Discussion

Salivary gland carcinomas represent 1–3 % of all head and neck malignancies**[3]**. Acinic cell adenocarcinomas (ACA) account for approximately 5 % to 11 % of these salivary gland cancers **[3]**. Eighty-six percent of ACA arises in the parotid glands, and its occurrence in the parapharyngeal region is rare **[4]**.

The mainstay of treatment for this tumor is surgery with or without adjuvant radiation therapy or chemoradiotherapy, with a 5-year overall survival of 88.6 %. Patients with high-grade tumors, regional metastasis, or positive resection margins typically confer a poorer prognosis. Regional metastases and high-grade histology were rare (8.2 %, 5.1 %) **[3]**.

The cavernous sinus is a rare site for ACA to metastasize to. In a review of 144 cases, Liu et al. **[4]** illustrated the efficacy of gamma knife radiosurgery in tumors involving the cavernous sinus, with a high tumor control rate and few complications. However, none of the 144 cases was a metastatic ACA to the cavernous sinus.

A review of the English literature revealed that there have only been 3 case reports of metastatic acinic cell carcinoma from the parotid gland to the cavernous sinus without direct extension of the tumor **[6-8]**, of which only 1 was treated with radiotherapy. Thottian et al. **[8]** reported a case of a 62-year-old male with metastatic ACA to the bilateral cavernous sinus who presented with ophthalmoplegia and headache. He subsequently received a radiotherapy dose of 20 Gray

in 5 fractions over 1 week with palliative intent and experienced resolution of the symptoms above. In the cases of Yildirim **[6]** et al. and Lin et al. **[7]**, the metastatic acinic cell carcinoma in the cavernous sinus was primarily treated surgically without radiosurgery.

In our case, the oral maxillofacial team had postulated that the primary correct para pharyngeal ACA had spread via perineural invasion of the adjacent mandibular division of the trigeminal nerve, which passed through the Gasserian ganglion and then into the posterior aspect of the right cavernous sinus. Direct connections between bilateral cavernous sinuses facilitated the contralateral spread of tumor cells and subsequently through to the division of the trigeminal nerve towards the left inferior alveolar canal **[9]**.

Due to the rarity of the case, published literature is scarce on treating metastatic acinar cell adenocarcinoma with Gamma Knife Radiosurgery. A case series reported eight patients who received gamma knife radiosurgery as a treatment for recurrent salivary gland malignancies. Only one of the eight cases had an ACA originating from the right parotid gland and metastasized to the left and right cavernous sinus, right sphenoid sinus, and right foramen ovale. The volume of the left large sinus lesion was 0.7cc, and the treatment dose was 18 Gy to the 50 % isodose line, while the importance of the right lesion was 1.3 cc and received 11 Gy/50 %. The left lesion showed progression after 2.3 months and was treated with repeat GKRS and had achieved local control after 16.8 months **[10]**. Other reports of utilizing GKRS as a boost after completion of neutron radiotherapy for salivary gland neoplasms involving the base of the skull showed some improvement in local control **[2,11]**.

| Author | Year | Paper design | Location of metastasis | Origin | Management | Outcome |
|---|---|---|---|---|---|---|
| Yildirim et al | 2005 | Case report | Right cavernous sinus | Right parotid gland | Surgical excision | No recurrence |
| Lin et al | 2013 | Case report | Left cavernous sinus | Left parotid gland | Surgical excision | No recurrence |
| Thottian et al | 2016 | Case report | Bilateral cavernous sinus | Right parotid gland | Palliative radiotherapy | Tumor control and resolution of symptoms |

## Conclusion

Based on our single case experience, metastatic Acinic Cell Adenocarcinoma appears to have responded well to Gamma Knife Radiosurgery. Although there was evidence of growth on serial imaging in the months that followed the first session of Gamma Knife Surgery, the second session of GKRS had proved efficacious in achieving tumor control. Further studies with larger sample sizes are needed to validate this finding.

This case report has highlighted the importance of close radiological surveillance of such a lesion, given its potential for asymptomatic recurrence. It also demonstrated the role of re-treatment with Gamma Knife Surgery, with a low risk of the associated side effects and complications.

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