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Recurrent Central Neurocytoma Treated with Robotic Radiosurgery

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ABSTRACT

Central Neurocytoma is a rare intraventricular neuroepithelial tumor (<1% of primary brain tumors). Surgical resection is the standard treatment, however 30-50% of cases result in subtotal resections. Due to its rare incidence, the therapeutic approach to disease persistence or local recurrence after surgery remains controversial. Recurrence of these tumors can be associated with intracranial bleeding, malignant transformation, or meningeal dissemination, making their local control a challenge. With the advance of radiotherapy techniques, it is estimated that it may play a significant role in the treatment of these tumors. We describe a case report of recurrent Central Neurocytoma effectively and safely treated with Cyberknife® Robotic Radiosurgery. After a follow-up of 81 months, the patient remains asymptomatic without signs of disease progression.

Keywords: *Central Neurocytoma, Cyberknife, Robotic Radiosurgery*

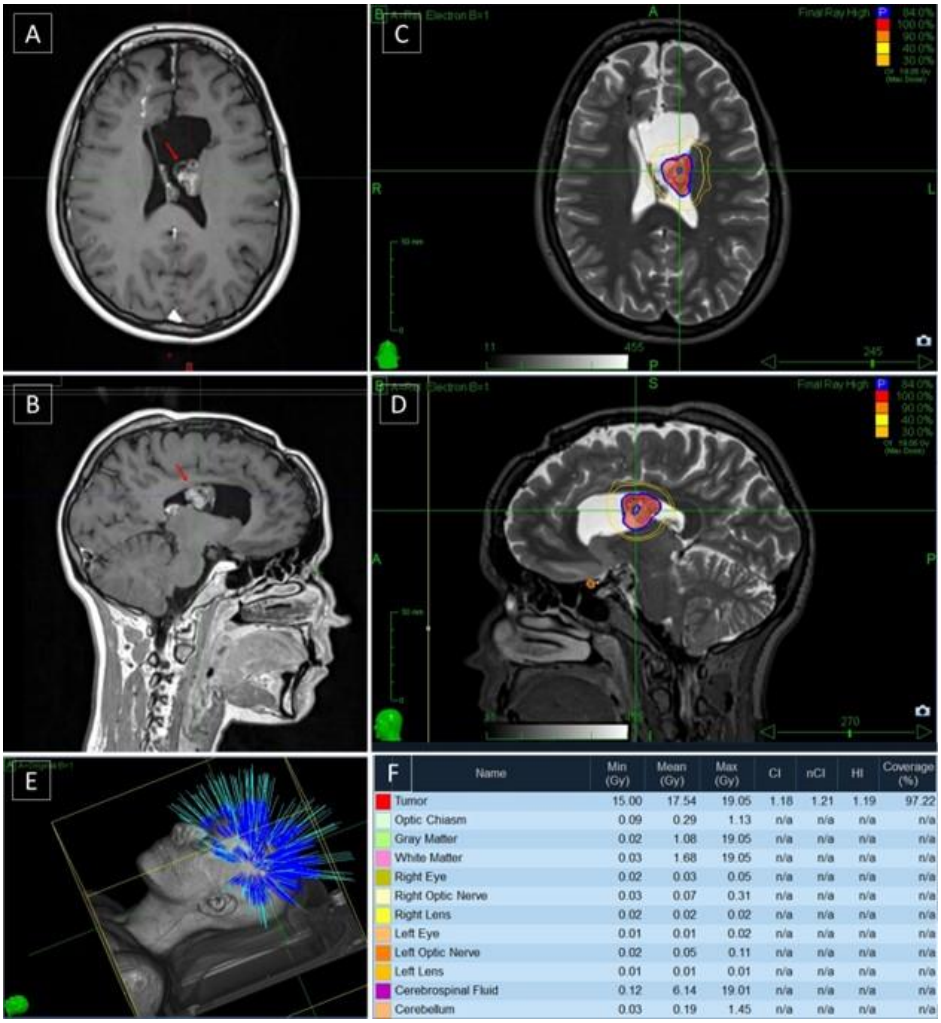
Introduction

Central neurocytoma (CN) is a rare entity, accounting for 0.25-0.5% of all primary brain tumors, and it originates from germinal matrix cells located in the septum pellucidum or periventricular region (E Park *et al*., 2012). CN are typically benign tumors, although malignant variations have been reported (Imber *et al*., 2016). The prognosis is generally favorable; however, it might exhibit aggressive behavior, especially with atypical variants (Song *et al*., 2016). Distinguishing CN from other brain tumors like ependymoma,

astrocytoma, intraventricular oligodendroglioma, or primary cerebral neuroblastoma can be challenging. A definitive diagnosis can only be made through immunohistochemistry to determine the neuronal origin of the tumor (Sharma *et al*., 2006). Although it's described that women at a younger age are more likely to have CN compared to men, current consensus suggests that both genders are affected equally (Alsadiq *et al*., 2022; Li *et al*., 2012). The tumor mainly affects young adults aged between 20 to 40 years old, with the peak incidence occurring in the third decade (Lee *et al*., 2016). The most common symptoms are severe headache, vomiting, and gait disturbance. Rare presentations include hemiparesis, seizures, and hemorrhage (Li *et al*., 2012). Surgery is the standard treatment approach; however, it might be challenging depending on CN size, its location in the deep midline close to critical intraventricular structures as well and its hypervascularity (Xiong *et al*., 2015). These limitations lead to the achievement of rates of complete resection only in 30-50% of the patients with CN (Lee *et al*., 2016). Radiotherapy is often reserved to treat recurrent and residual tumors (Patel *et al*., 2013). Due to its rarity, there is a lack of consensus or official guidelines for CN, particularly concerning new approaches involving modern radiotherapy techniques. We present a case of a 39-year-old female patient diagnosed with recurrent CN that was safely and efficiently treated with robotic stereotactic radiosurgery (SRS).

Case Report

A female patient, 39 years old, with no relevant personal medical history, sought a Neurosurgery appointment in 2006 due to persistent headaches. Brain magnetic resonance imaging (MRI) revealed a lesion with a cystic component in the frontal horn of the left lateral ventricle. She underwent frontoparietal craniotomy in two surgical stages, the first complicated by hemorrhage. The postoperative period was uneventful, and she presented asymptomatic with no neurological deficits. Anatomopathological examination and immunohistochemical profiling disclosed the histological diagnosis of Grade II Central Neurocytoma according to the WHO CNS tumors classification. The patients maintained clinical and radiological stability for 10 years after surgical intervention. In May 2016, a cranial MRI disclosed tumor recurrence adjacent to the ependymal surface of the left lateral ventricle, measuring approximately 2.2 x 1.6 cm in anteroposterior and transverse dimensions. In a multidisciplinary group meeting, ablative treatment with radiosurgery was proposed. In June 2016, she underwent robotic radiosurgery using the Cyberknife® robotic system, delivering a dose of 16 Gy applied in one single fraction through 181 beams, with dedicated Multiplan 6D-Skull® dosimetric planning. All organs at risk remained within dose constraints for radiation tolerance (Fig. 1). The treatment proceeded without complications and with good tolerance. Subsequently, she remained under periodic clinical and radiological surveillance. The patient did not undergo any systemic treatment throughout the entire process. After an 81-month follow-up, the patient remains asymptomatic with no radiological signs of recurrence or disease progression (Fig. 2).



Name	Min (Gy)	Mean (Gy)	Max (Gy)	CI	nCI	HI	Coverage (%)
Tumor	15.00	17.54	19.05	1.18	1.21	1.19	97.22
Optic Chiasm	0.09	0.29	1.13	n/a	n/a	n/a	n/a
Gray Matter	0.02	1.08	19.05	n/a	n/a	n/a	n/a
White Matter	0.03	1.68	19.05	n/a	n/a	n/a	n/a
Right Eye	0.02	0.03	0.05	n/a	n/a	n/a	n/a
Right Optic Nerve	0.03	0.07	0.31	n/a	n/a	n/a	n/a
Right Lens	0.02	0.02	0.02	n/a	n/a	n/a	n/a
Left Eye	0.01	0.01	0.02	n/a	n/a	n/a	n/a
Left Optic Nerve	0.02	0.05	0.11	n/a	n/a	n/a	n/a
Left Lens	0.01	0.01	0.01	n/a	n/a	n/a	n/a
Cerebrospinal Fluid	0.12	6.14	19.01	n/a	n/a	n/a	n/a
Cerebellum	0.03	0.19	1.45	n/a	n/a	n/a	n/a

Figure 1: A and B - Axial and Sagittal MRI T1 sequence with gadolinium, respectively (the red arrow points to the CN location); C and D - Axial and Sagittal view of Cyberknife radiosurgery treatment planning and isodose curves; E -Cyberknife treatment beam geometry; F - Dose distribution at the Tumor and Organs at Risk. (Min - Minimum; Max - Maximum; CI - Conformity Index; nCI - Normalized Conformity Index; HI - Homogeneity Index; Gy - Gray).

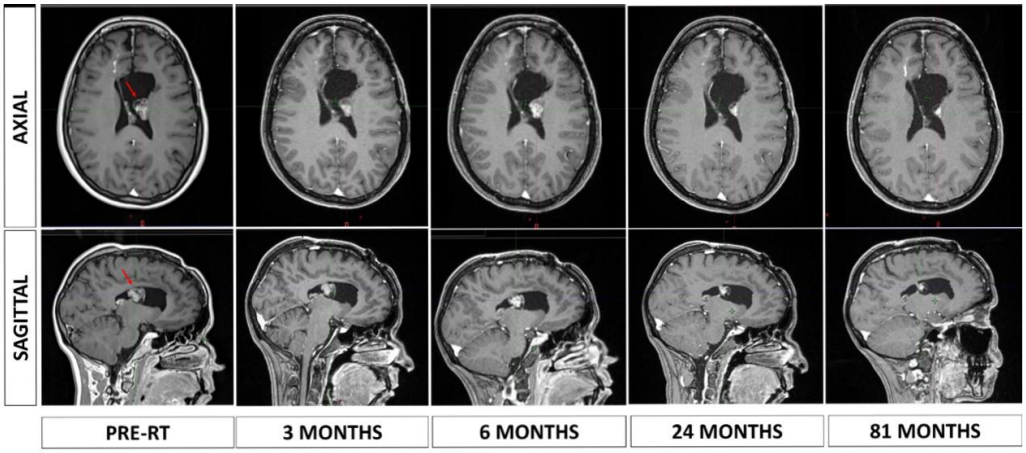


Figure 2: Axial and Sagittal MRI T1 sequence with gadolinium pre-treatment; At 3, 6, 9, 24, and 81 months after Cyberknife Radiosurgery. The red arrow points to the CN location.

Discussion

CN consists of an uncommon intraventricular tumor that manifests mainly in young adults, although it can also affect individuals across different age groups (Sharma *et al*., 2006). Cranial MRI might reveal a heterogeneous isointense or slightly hypointense masse on T1-weighted and isointense to hyperintense on T2-weighted imaging (Jaiswal *et al*., 2011). Surgery is the standard treatment, and it depends on the size and location of the tumor, adherence to adjacent structures, and experience of the Neurosurgeon (Choudhari *et al*., 2009). The primary objectives of the surgery are to achieve maximal tumor resection with minimal neurological consequences, obtain a specimen for a definitive histopathological diagnosis, and restore cerebrospinal fluid flow (Patel *et al*., 2013). Gross-total resection (GTR) is the gold standard treatment for CNs, however, is only achievable in 30-50% of patients. An extensive tumor resection entails an aggressive surgical approach that must be carefully balanced to mitigate the risk of neurological deterioration (Xiong *et al*., 2015). The 5-year survival rate of a GTR and subtotal tumor resection (STR) is 99% and 86%, respectively (Xiong *et al*., 2015; Elayouty *et al*., 2018). Subtotal resection is associated with an increased recurrence rate and when performed, adjuvant radiotherapy has proved to significantly improve local control (LC), progression-free survival (PFS), and overall survival (OS) (Samhouri *et al*., 2021). A multicentric analysis published in 2021 reported the results of 33 patients with CN submitted to surgical resection followed by conventionally fractionated radiotherapy (CFRT) administered in a median total dose of 54 Gy. They reported an overall 5-year OS of 90% and a 5-year PFS of 76%. Patients who received radiotherapy had a significantly longer PFS than patients without RT and a trend towards longer OS (Samhouri *et al*., 2021). SRS has allowed a favorable profile for the management of CNs, with high rates of local tumor control and low risks of symptomatic complications when compared to CFRT (Rades and Schild, 2006; Garcia *et al*., 2014). Some studies published in the literature assessed the role of SRS in the treatment of recurrent CN, in the majority after a previous STR (Genc *et al*., 2011; Chen *et al*., 2011; Karlsson *et al*., 2012; Kim *et al*., 2013; Chen *et al*., 2014; Pan and Lee, 2015; Yamanaka *et al*., 2016; Lee *et al*., 2018). Patients were treated with the Gamma knife radiosurgery (GKRS) technique, with a median therapeutic dose ranging between 12 to 16 Gy. The local control rates were 90-100% at 5 years and 80-90% at 10 years, respectively, with patients who underwent GTR experiencing better progression-free survival (PFS) and local control. To determine the optimal treatment for recurrent or residual intraventricular neurocytomas, in 2014 Garcia and colleagues published a systematic review comparing CFRT versus SRS. The local tumor control was 93% and 88% in the SRS and CFRT subgroups, respectively. The relative risk of local recurrence was 0.57 less in the SRS subgroup compared to the CFRT, although it did not reach statistical significance (95% CI: 0.21 -1.57; log-rank p = 0.85). Lower toxicity was noted for patients treated with SRS although distant tumor recurrence tended to be slightly higher in the SRS subgroup (1.5% versus 5.5%, p = 0.24) (Garcia *et al*., 2014). Recently, Hung, *et al*. (2020) performed a multicenter, retrospective study, to

evaluate the outcomes of SRS with CNs and identify predictive factors. The study comprised 60 patients, 92% of whom had undergone prior resection or biopsy. Patients were treated with a median margin dose of 13 Gy. After a median follow-up of 61 months, post-SRS, the tumor recurrence occurred in 8 patients (13%). The 5- and 10-year LC were 93% and 87%, respectively. The 5- and 10-year PFS were 89% and 80%, respectively. Adverse radiation events were observed in 4 patients but only 1 was symptomatic, presenting transient diplopia. Prior radiotherapy was a predictor of distant tumor recurrence ($p = 0.044$) and larger tumor volume was associated with pre-SRS shunt surgery ($p = 0.022$) (Hung *et al*., 2020). Our report illustrates a case of a patient diagnosed with a relapse of a CN 10 years after surgery, who underwent treatment with robotic radiosurgery. After a long follow-up period (81 months), she remains with no evidence of progression. Considering the focal and well-defined characteristics of the majority of CNs, SRS may represent a significant treatment choice in addressing these lesions.

Conclusion

We present a case study of a 39-year-old female patient diagnosed with recurrent CN who underwent treatment with Cyberknife Robotic Radiosurgery. The treatment was very well tolerated and after a follow-up of 81 months, there is no evidence of clinical or imagological relapse or progression. Due to the rarity of CN, the existing literature on the role of modern radiotherapy techniques is limited. Further studies are needed to establish specific guidelines for the management of CN.

Abbreviations

CFRT - conventionally fractionated radiotherapy
CN - central neurocytoma
GKRS - Gamma knife radiosurgery
GTR - gross-total resection
LC - local control
MRI - magnetic resonance imaging
OS - overall survival
PFS - progression-free survival
SRS - stereotactic radiosurgery
STR- subtotal resection

Ethical Approval and Consent to Participate: All procedures were performed in accordance with the Ethical Standards of the Institutional and National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Formal consent for the publication of this study was granted.

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1. Conception and design: Marina Amorim; Adelina Costa
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3. Manuscript writing: Marina Amorim, Adelina Costa, Cármen Calçada
4. Final approval of manuscript and agreement to be accountable for all aspects of the work: Paulo Linhares, Paulo Costa

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