The Management of Central Neurocytoma
Radiotherapy

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KEYWORDS

• Central neurocytoma • Radiation • Irradiation • Radiotherapy • Management

KEY POINTS

- Adjuvant stereotactic radiosurgery (SRS) or conventional radiotherapy (cRT) for neurocytoma leads to long-term local control rates in excess of 85%.
- The relative risks of local recurrence and all-cause mortality after SRS for neurocytoma are slightly less than with cRT, but not statistically significant.
- Neurocytoma recurrence after radiotherapy is significantly associated with histologic atypia, but not extent of resection or radiation modality.
- Severe complications are slightly less common in neurocytoma patients treated with SRS, relative to cRT.
- Distant tumor recurrence is slightly lower in neurocytoma patients treated with cRT, relative to SRS.

INTRODUCTION

Central neurocytomas or intraventricular neurocytomas (IVNs) originating in the ventricular space were first recognized by Hassoun and colleagues[1] in 1982. These tumors of neuronal differentiation are rare, accounting for 0.1% to 0.5% of all primary brain tumors,[2,3] and, while they tend to be benign, malignant variants have been reported. For these tumors, microsurgical resection remains the standard of care. However, the management of residual or recurrent tumors remains controversial. Recurrence of these benign lesions raises doubt about the utility of conservative management.[4,5] For this reason, some authors advocate routine use of adjuvant therapy, such as radiotherapy or chemotherapy, for cases of incomplete surgical resection or IVNs with atypical histologic characteristics. These selective recommendations are driven by concerns of radiation-related morbidity, including neurocognitive decline, radiation necrosis, and secondary malignancy risk.[6–8]

ADJUVANT RADIOTHERAPY OPTIONS FOR NEUROCYTOMA

Overview

Two common adjuvant therapeutic strategies for incomplete or recurrent IVNs include conventional radiotherapy (cRT) and stereotactic radiosurgery (SRS). Before the era of SRS, fractionated cRT was a common noninvasive approach used to manage incomplete or recurrent lesions. More institutions have since adopted SRS for adjuvant therapy, given the relatively higher efficacy and lower long-term risks.[9–11] However, the adjuvant therapy that offers a higher safety and local control rates remains unclear. In January 2012, Park and Steven[11] performed the first systematic quantitative review of the efficacy of SRS for local control of IVNs. The authors identified 5 studies with a total of 64 IVNs and found a single session of SRS was a safe and effective therapy. Most IVNs included in the study had undergone surgical resection, but 13% of subjects had

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undergone only biopsy, or SRS was the primary treatment. The last meta-analysis conducted on SRS versus cRT for incompletely resected neurocytomas was done in 2006.[9] The authors found no statistically significant differences in 5-year local control rates between the cRT and SRS cohorts ($P = .45$).

Since the aforementioned publications, several new case series have been reported[12–20] and older case series have been updated to include more subjects and longer follow-up.[21–25] Here, the primary literature concerning the use of adjuvant radiotherapy for neurocytoma spanning the past 30 years is systematically reviewed, with an emphasis on cRT technique, efficacy, and complications. Studies concerning SRS for neurocytoma are summarized for comparison in an effort to provide comprehensive treatment recommendations for the adjuvant management of neurocytoma. Tables 1 and 2 summarize select high-quality articles documenting treatment characteristics and clinical outcomes of neurocytoma patients who were treated with adjuvant radiotherapy. Additional studies that were not included in a meta-analysis for the indicated reasons are summarized in Table 3. A summary of patient demographics and IVN factors associated with treatment subgroups is provided in Table 4.

Radiation Dose

The mean marginal (peripheral) dose of Grays (Gy) that subjects received in the SRS subgroup was 14.9 Gy (standard deviation [SD] = 3.2; range 9–25 Gy). The mean total dose subjects received in the cRT group was 53.0 Gy (SD 11.52; range 20–84 Gy). Tables 1 and 2 provide summaries of radiation parameters and protocols for each study.

CLINICAL OUTCOMES

Local Control

Among the cases summarized in Tables 1 and 2, overall local control was 91%, with 14 recurrences of 158 pooled IVNs (Fig. 1). The mean time to disease progression was 41 months (range: 18–67). The local control proportion among the SRS and cRT subgroups was 93% and 88%, respectively. Six recurrences were observed in the SRS subgroup (n = 91) and 8 in the cRT subgroup (n = 67). Although the risk of recurrence was marginally less in patients who received SRS, the difference was not statistically significant nor was the risk of recurrence dependent on extent of resection. In contrast, the proportion of recurrences varied significantly with histologic atypia.

Survival

The overall proportion of survival was 94%, with 9 deaths identified of 155 subjects (Fig. 2, see Tables 1 and 2). The median time to death was 104 months (range: 13–227 months), and the surviving proportions for SRS and cRT subgroups were 98% and 90%, respectively. Although the differences were not statistically significant, 2 deaths were observed in the SRS subgroup (n = 88) and 7 in the cRT subgroup (n = 67). The single death reported by Yen and colleagues[14] was in a 37-year-old woman treated with gamma knife (GKS; 18 Gy marginal dose) who died 13 months after the procedure secondary to sepsis following a shunt obstruction and infection. All other deaths reported were due to tumor progression or long-term risks of cRT except for the Leenstra and colleagues[22] 2007 study, wherein the authors only presented group level data on deaths. In particular, 7 subjects died of causes not directly related to tumor progression (3 cerebral edema, 4 pulmonary embolism, 2 ventriculoperitoneal shunt infections, and 1 pneumonia) and 1 additional case developed recurrence at 4 months postoperatively and succumbed to brain infarction 1 month later. Notably, it is unclear which of these subjects received adjuvant cRT.

The Paek and colleagues[34] 2008 study had the longest follow-up time for the cRT subgroup and reported 2 deaths. One 25-year-old man died because of chronic progressive neurologic deterioration caused by radiation necrosis 227 months after cRT and a second 25-year-old man in the series died following brainstem compression caused by a radiation-induced meningioma 206 months after radiotherapy. The other causes of deaths reported include neurologic damage induced by tumor progression with intracranial hemorrhage at 40 months after GKS[15] and tumor progression at 36 months in a patient with MIB-1 labeling index greater than 4% following partial resection and cRT.[33]

COMPLICATIONS AND CONCERNS

A full listing of all complications by study is detailed in Table 5. There was no difference in serious treatment-associated toxicity between SRS and cRT neurocytoma patient subgroups, but 3 total studies reported radiation-induced adverse events.[15,28,52] Martín and colleagues[28] described one patient with both acute (alopecia) and chronic (radiation necrosis and edema 2 years after treatment) adverse events related to radiosurgery. The chronic adverse events resolved following ventriculoperitoneal shunt implantation and corticoid treatment. Three subjects with 4